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THE MORPHOLOGY AND HISTOLOGY OF A HUMAN EMBRYO  
OF 8.5 MM. By H. L. BARNIVILLE, B.A., M.B., *Demonstrator of  
Anatomy in University College (N.U.I.), Dublin.*

## INTRODUCTION.

THE embryo which is the subject of the following investigation was obtained in January 1913 in the Frauenklinik at Giessen (director, Professor Opitz) by operation on a woman in whose case an excision of the uterus was rendered necessary on account of tuberculosis, and came into the hands of Professor Keibel through the kindness of Dr Jaschke. It is now included in the Keibel series as No. 1495 at the Anatomical Institute of the University of Freiburg in Breisgau. The embryo came into the fixing fluid in an exceedingly fresh condition; and, when a series had been made, proved to be in such an excellent state of preservation that I undertook, at Professor Keibel's suggestion, a description of the whole anatomy, with the intention of making it as complete as possible as far as the more interesting points were concerned. Accounts of the morphology of individual embryos have been frequent in the literature since the time of His; and although a certain amount of overlapping must obviously occur in the observations of various authors, the value of such work is none the less very appreciable. An accurate idea of a given stage in the development of an organ or part cannot be scientifically founded on a single description; and just as our knowledge of adult morphology has been built up by the combination of often very divergent interpretations of a given condition, in the same way must our data, with regard to the course of embryological evolution, be raised to a higher plane of scientific accuracy by the elimination of the personal factor in the equation.

Of recent years two papers have appeared which have a special bearing on the present research—that of Ingalls on a 4.9-mm. and that of Elze on a 7-mm. embryo; and any subsequent worker along the same lines must necessarily feel himself more especially indebted to these two exhaustive

references, providing as they do not only many valuable suggestions but also a definite guide in the treatment of an otherwise somewhat diffuse subject.

The methods employed were those already described in the literature and applicable in a work of the kind. The embryo was fixed in a sublimat-picric acid fluid, and after being photographed (Plate I. fig. 1) was embedded in celloidin-paraffin. The block was provided with guiding lines after the glass-box method of Born and Peter, cut in series with a sectional thickness of  $10\mu$  and stained with eosin-azure. The resulting sections are of excellent quality, and provide a well-nigh perfect histological picture, with numerous mitotic figures and a normal condition in the contour of the epithelial linings of the various organs, vessels, and body-spaces. The nerve trunks, although their constituent fibres remain unstained, are sharply defined owing to the characteristic appearance of the sheath-cells, as well as the contrast afforded with respect to the surrounding mesoderm, and can be followed to their ultimate terminations. Figs. 7 and 8 on Plate II. will provide an idea of the condition of the cellular histology under high magnification. Small but comparatively unimportant folds occur in some of the sections. The plane of section is not quite horizontal, as will be seen from the text figures, so that the left side of the latter (representing the right side of the embryo) pictures in each case a level somewhat oral in respect to the right side. Graphic profile reconstructions were made of the various systems (figs. A, B, and C), after the methods employed and described by different workers and epitomised by Peter in his *Methoden der Rekonstruktion*. The left side of the embryo was in each case taken as the basis of the reconstruction, but in at least one case a condition occurring in the right side and absent on the left was added in, viz. the connexion between N. IX. and N. X. A few reconstructions from an antero-posterior aspect were also made in the case of some of the organs, viz. the anlage of the lung, in order to obtain a more definite picture of their condition than was possible merely from a study of the sections or from a lateral reconstruction. The guiding-line system employed was two-fold, in some cases both being utilised for comparison and to eliminate errors; on other occasions one or other separately was found to be the more accurate. These were: (a) the guiding lines of the block combined with those which were subsequently drawn on the individual outlines of the sections, and (b) the outline of the whole embryo obtained by an enlargement of the photograph by means of the projection apparatus. Such reconstructions, as has often been pointed out, are not to be regarded as quite free from error even with the most accurate manipulation of the guiding lines, but the results obtained are such as cannot be so conveniently

produced by other methods, and indeed, as for instance in the case of the arterial and venous systems, are almost impossible of achievement by the wax-plate method. A comparison of the reconstructions with the text figures will further show that discrepancies are practically absent, and where such are found they will prove to be so minimal as to be negligible for all practical purposes. Wax models after the Born method were prepared of some of the individual organs, and are reproduced in the drawings on Plates I. and II. The text figures were drawn direct from the projection apparatus, and are faithful in outline and detail.

#### LENGTH OF THE EMBRYO.

The embryo, measured from the photograph in which it was subjected to a definite known enlargement, has a greatest length of 8.5 mm. When embedded and cut it provided a series of 840 sections of  $10\mu$ , so that shrinkage, if any, has been very slight. According to Mall's method of reckoning, the embryo would thus have reached the early part of the thirtieth day of its development. In view, however, of the conclusive researches of Bryce, a correction must be made of the Mall formula, viz. the addition of five days to the age, which would place our embryo quite at the end of the fifth week.

#### EXTERNAL BODY-FORM.

The embryo, as seen from the photograph (Plate I. fig. 1), falls between figs. 9 and 10 of the *His Normaltafel* and between figs. xiii. and xiv. of the *Normaltafel* of Keibel and Elze, resembling the former more closely than the latter. Fig. xiii. is of the embryo (7 mm. *ca.*) which has been the subject of a full description by Elze, and which will be frequently referred to in the following pages. A comparison with that figure, however, will show that the present embryo shows an advancement in many particulars. It is not so curved on itself either cranially or caudally, although the cervical bend is very sharp and approaches a right angle. On the outer surface of the head region the cerebral hemispheres, the optic cup and lens, and the roof of the fourth ventricle show up distinctly. Behind the eye and above the maxilla and mandible is the swelling of the trigeminal ganglion, and still further back above the hyoid arch is the swelling caused by the otic vesicle, with the ductus endolymphaticus continued dorsally from it lateral to the roof of the hind-brain as a very apparent streak. The nasal pit looks laterally as well as towards the heart, and the lateral and medial nasal processes being more prominent, it is deeper than in Elze's embryo. Three visceral arches are to be distinguished. The mandibular arch is subdivided by a horizontal groove into two swellings, while its maxillary process takes a

definite part in completing the margin of the nasal pit. It shows further a secondary vertical groove which runs almost parallel with the nasolacrimal groove and ends dorsally caudal to the optic anlage (see Plate I. fig. 3). This groove first appears in fig. xv. *r.* of Keibel and Elze's Normaltafel, and is seen in fig. xviii. from the same source, reproduced as fig. 49 of Keibel and Mall's *Text-book*, vol. i. The hyoid arch is also subdivided by a horizontal groove, and has an opercular prolongation continued caudally from it. The first branchial arch is sunken into the sinus cervicalis, which still possesses a wide triangular opening. The placode formations in connexion with N. IX. and N. X., or, more strictly, the openings of the ductus branchialis II. and ductus branchialis IV., can be seen on the surface anterior and posterior to the third arch respectively. In the anterior extremity an oval hand-plate and short forearm, and in the posterior an oval foot-plate are to be recognised. The axis of each limb is set at an oblique angle with respect to the dorsal line. The segmented muscle plates and sclerotomes are very obvious in the dorsal and caudal regions. The tail is spirally twisted on itself and is curved towards the left of the umbilical cord, which maintains a more or less medial position. The heart swelling does not quite reach the cord, and is more definitely marked off from the liver than in fig. xiii. above referred to. There is furthermore a slight surface demarcation between the auricular and ventricular sections of the heart in the form of a short groove or pit about midway along the groove separating the two organs.

#### NERVOUS SYSTEM.

*The Brain.*—The morphology of the brain, as seen in outline in the profile reconstruction (fig. A), shows a general similarity to that of the well-known His model of a fourth-week embryo (6.9 mm.), and that of Elze (7 mm. *ca.*). A few points may, however, be noted as marking an advancement. The anlage of the cerebral hemispheres is more pronounced, but a partial separation of the two halves is as yet indicated merely by a shallow fossa (fig. 9), at the bottom of which is a low ridge. On the floor of the diencephalon are seen the mammillary and infundibular swellings, and more anteriorly a less well-marked swelling—the torus opticus. Between the two latter is a shallow pit where the hypophyseal pocket lies against the brain-floor. On the roof of the mid-brain, in the middle line and in the position marked by an arrow (fig. A), is a small area, extending over about four sections ( $10\mu$ ), in which the structure of the brain-roof differs from the general type (fig. 1). The outer aspect of the brain-wall shows a small, nipple-like projection, corresponding with which, on the inner surface, is a shallow pit. The wall of this recess



consists of radially arranged cells, of which the nuclei, in marked contrast to the rest of the neural tube, are confined to the outer layers, leaving an inner protoplasmic layer free from nuclei. In the junctional zone between this projecting area and the normal brain-wall are numerous darkly

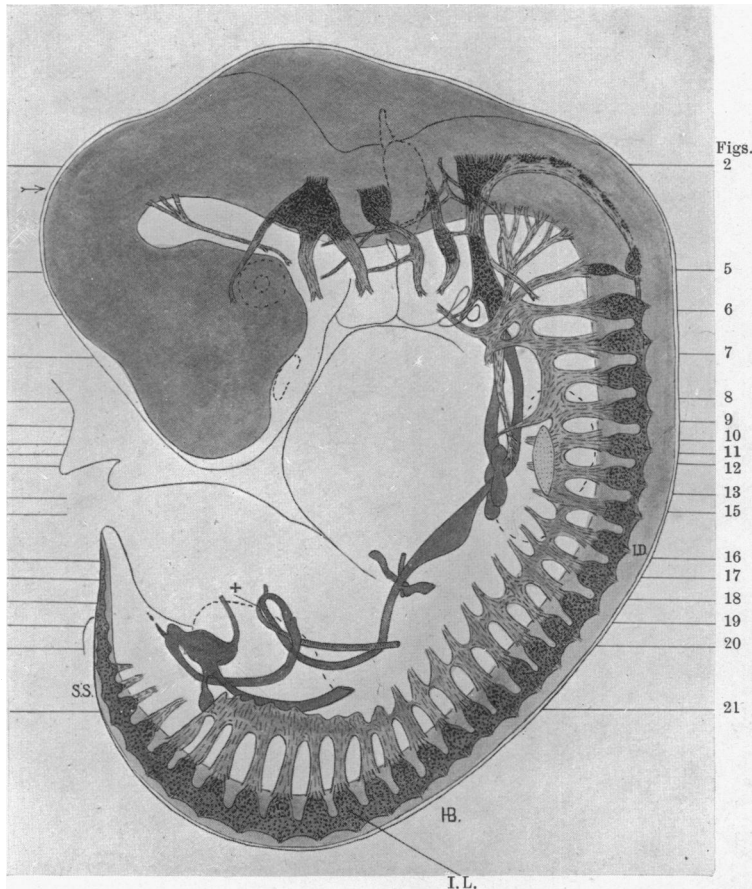


FIG. A.  $\times 12\frac{1}{2}$ .

staining nuclei. This finding corresponds exactly in its appearance with the structure described in a similar position by Elze (7 mm.), and in its histology with the description given by Mihalkovics of the histology of the early pineal outgrowth. There can be little doubt that it represents the early anlage of this structure. The isthmus is well marked. The very thin roof of the rhombencephalon has become invaginated into the ventricle

during embedding. The side wall and floor have well-marked neuromeres, though the most posterior is short and is seen only dorsally at the level of the origin of the vagus (fig. 2). The neuromeres are most marked on the inner face of the brain-wall in the form of grooves, but they involve also the mantle layer. The first has no nerve-root in connexion with it, and constitutes the cerebellar neuromere. It blends below with the second neuromere (or "first" neuromere proper, according to Streeter's reckoning). The relation of the various cranial nerves to these structures is essentially that described by Streeter, etc., for man, except in the case of N. VI., which does not arise exclusively from the fourth neuromere (*cf.* below). Early

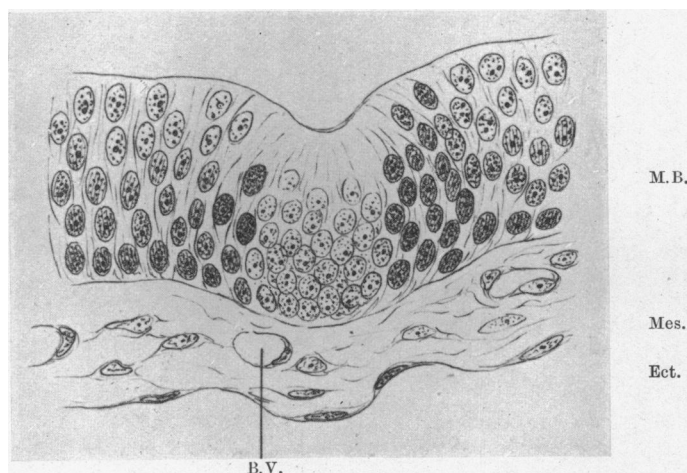


FIG. 1.  $\times 1500$  ca.

indications of some of the future tracts in the rhombencephalic wall are indicated. In the marginal zone of the floor numerous transversely coursing fibres mark the "Bodenkommissur," and on either side, near the mid-ventral line, is a group of longitudinal fibres—the future median longitudinal bundle. The entering fibres of N. V. sweep in part forwards and upwards, and although, owing to absence of staining, they cannot be traced clear of the first neuromere, may probably indicate an early tractus cerebelli V. Other fibres take a backward direction, as is the case with the cranial nerves generally, the entering fibres assuming in part a longitudinal direction in the reticular marginal zone, without forming definite tracts except perhaps in connexion with N. X. Immediately above the longitudinal fibres the marginal zone diminishes in thickness and almost disappears, exactly as is seen in the spinal cord dorsal to the posterior funiculus.

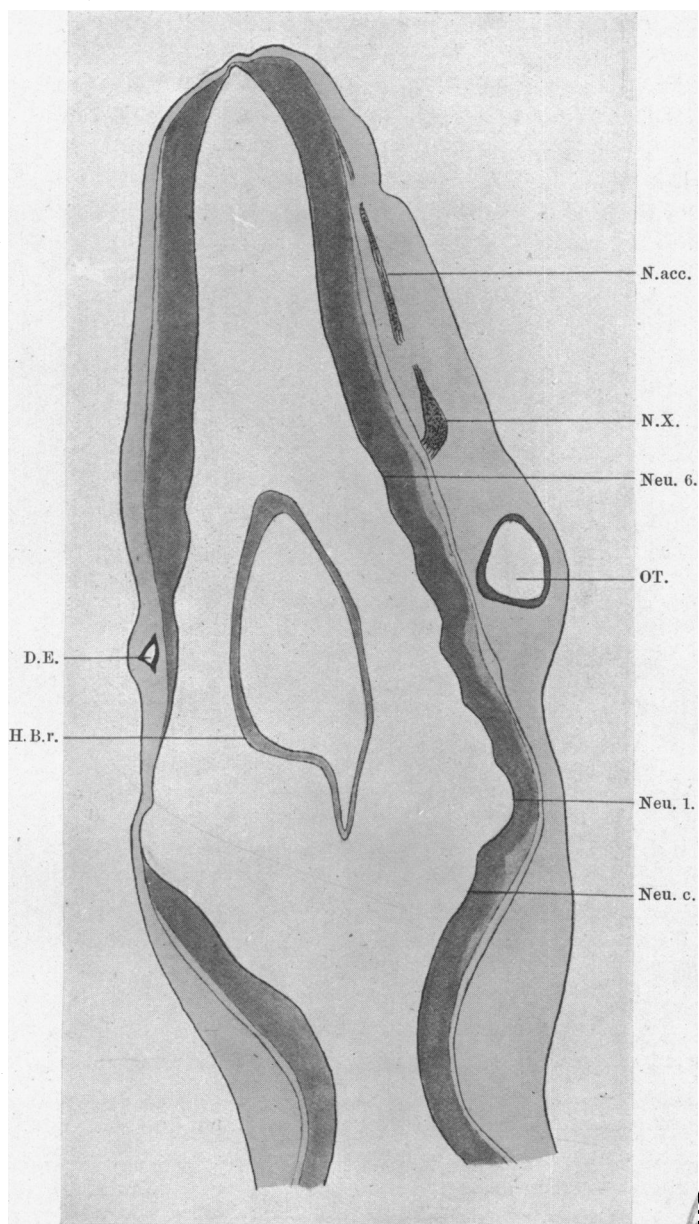


FIG 2.  $\times 30$ .



*Spinal Cord.*—The lumen of the neural tube can be followed to within four sections ( $10\mu$ ) from the caudal tip, the tube itself blending aborally with the epithelium covering the tip. The wall in this region consists of a single layer of high columnar cells, as Lenhossék describes; the only suggestion of layer-differentiation is the frequent appearance of mitotic figures in the nuclei of the innermost zone. Near its caudal termination the lumen contains two large clumps of degenerating cells attached to the roof of the tube and extending in each case through about ten sections (fig. 20). Elze (7 mm.) has described similar groups of cells lying free in

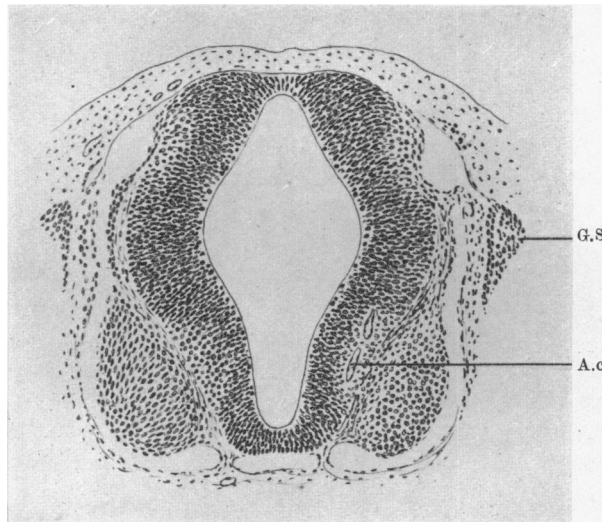


FIG. 3.

the lumen. Here can be most conveniently included a short account of the condition of differentiation of the wall of the neural tube in general. An examination, for example, of a section passing through the upper cervical region (fig. 3) shows that the wall may be divided for descriptive purposes into three main layers. This condition is best marked in the region of the anterior horn anlage. Internally is a broad layer of darkly staining nuclei and radially arranged protoplasmic filaments, the whole affording the usual radially striated picture of early stages. Its inner zone shows numerous mitotic figures (germinal layer). Outside this layer is the clump of anterior horn nuclei, less darkly staining and having no radial arrangement. Between these two is a thin layer of circumferentially arranged oval nuclei and fibres—the “zona arcuata” of His. This arcuate

zone is continued dorsally internal to the posterior longitudinal fibre-bundle around which the nuclei become more numerous, constituting an early posterior cell column (His). This zone of fibres and cells forms a markedly differentiated mantle layer, but it is not the sole expression of the process of differentiation in this layer. The outer zone of the radially striated layer shows a loosening up of its structure ("aufgelockerter Theil" of His) inasmuch as the nuclei are less radially arranged, set farther apart, and stain as a whole less deeply than in the rest of the layer. This process is scarcely noticeable in the region of the sulcus limitans, but is well seen dorso-mesial to the posterior longitudinal fibre bundle, and more particularly opposite the anterior horn anlage, the latter having the appearance of "invading" the inner layer across the barrier of the zona arcuata. This loosened zone is then discontinuous dorso-ventrally, in contrast to the arrangement figured by His, and the appearances indicate that this further differentiation of the mantle layer occurs earliest in the two above-mentioned situations. The outermost layer is quite free from nuclei, and consists of fibres running in various directions, giving it a reticular structure. It is thickened antero-mesial to the anterior horn—the funiculus anterior, and opposite the entrance of the posterior root fibres—the funiculus posterior; dorsal to this it is absent. A well-marked anterior commissure is present, and derives its fibres mainly from the zona arcuata. Some of the fibres, however, do not cross, but sweep around the mesial aspect of the funiculus anterior to remain on the same side of the cord. Traced headwards the anlage of the funiculus posterior fades away a short distance anterior to ganglion C. I. Caudally it can be traced as far as the second sacral segment, beyond which a definite anterior horn also becomes indistinguishable—although ventral root fibres arise down to the level of the first coccygeal segment. The anterior horn anlage traced orally can be followed into the rhombencephalon as a thickening of the differentiated mantle layer, from which the rootlets of N. XII. arise. The remainder of the wall of this portion of the brain consists of a radially striated layer with its inner germinal zone of mitotic figures and a loosened outer zone, and enveloped by a reticular layer containing the fibre tracts above described. The fore-brain is lined by a radially striated layer quite undifferentiated dorsally and laterally, but ventro-laterally there is a slight loosening-up process apparent in the outer zone, here covered by a thin clear layer free from nuclei.

*Cranial Nerves.*—The general arrangement of the cranial nerves, as seen in the profile reconstruction (fig. A), corresponds with Elze's (7 mm.) description, and in the case of N. IX., X., XI., and XII. with the account given by Streeter for embryos about this age.

N. III. arises by a large number of fasciculi from the floor of the mid-brain. In its course it runs internal to the "vena capitis medialis" (Grosser), and to the ophthalmic division of N. V., with which latter it is in connexion, as will be later referred to under N. V. It ends in two terminal branches in a well-defined mass of condensed mesenchyme in which N. VI. ends more posteriorly. This is the anlage of the orbital pre-muscle mass, and lies postero-dorsal to the optic cup and external to the A. carotidis interna. The nerve shows no ganglion cells along its course. Of N. IV. no part could be definitely recognised either in its intra-cerebral or peripheral course. The non-discovery of this nerve after careful searching must be ascribed to its small size, the undifferentiated condition of its nuclei, and more particularly to the fact that it would be cut transversely throughout its whole course. Elze notes only the crossing of the fibres in the roof of the brain, and fails to find any trace of its peripheral fibres.

N. V.—The central fibres of the trigeminal ganglion, on entering the marginal zone of the brain-wall, run in three main directions: one set makes directly for the mantle cells of the first neuromere,<sup>1</sup> and probably also of the second; another set runs longitudinally backwards, constituting the anlage of the spinal root V.; while a third set can be traced some distance forwards. The motor root arises some distance ventrally and becomes closely applied to the inner face of the ganglion, but remaining quite distinct from it. The ganglion in its upper part is dorsal to the vena capitis; lower down it comes to lie lateral to and closely opposed to this structure. It gives off three branches along which ganglion cells are carried for some distance. Especially is this the case with the ophthalmic branch, the root of which constitutes a finger-like process of the ganglion. This process is not distinct (as Elze) from the origin of the nerve. The ophthalmic nerve runs forward over the optic cup, crossing external to N. III., and curves downwards, keeping close to the circumference of the cup as indicated in fig. A. The detail of this branch and its relation to N. III. can be followed only with difficulty owing to the faintness of its loosely arranged fibres, but the following further points can be made out. On the right side, after crossing N. III., it expands in its sectional area. This expansion is due to a sprouting from its mesial surface, from which a branch runs through about seven sections ( $10\mu$ ) internal to the main trunk. The point of origin of this branch is separated from the anterior branch which N. III. drops down into the orbital pre-muscle mass by the anterior pole of this structure, and from this division of N. III. a small

<sup>1</sup> In the following account the neuromeres are reckoned exclusive of the first or "cerebellar" neuromere. Thus neuromere 1 is "neuromere a." of Streeter and "neuromere 2" of v. Kupffer, Bradley, Gräper, etc. See fig. 2.

fibre-bundle can be traced a short distance in the direction of the ophthalmic nerve. No ganglion cells are to be seen, but the picture suggests an early naso-ciliary branch with a commencing ciliary system. On the left side is a similar sprouting of the ophthalmic nerve, without a definite branch, and the arrangement of the mesodermal cells suggests a fibre connexion between it and N. III. Nervi mandibularis and maxillaris can be continued far into the first arch and its maxillary process respectively. The latter branch on approaching its termination is broken up into bundles by cells which, though mostly of the "sheath" type, are in part of ganglionic appearance. Its relation to the great superficial petrosal nerve will be later referred to. N. mandibularis shows no branching except for a short stump-like branch from its outer aspect twenty-five sections ( $10\mu$ ) from its origin. It receives the entire motor root.

Near its termination the nerve passes through a tunnel of strongly condensed deeply staining mesoderm, which is prolonged distally gutter-like along its outer and posterior aspect—the anlage of Meckel's cartilage. A portion of the nerve, however, splits off and runs a short distance on the outer side of this anlage. The chorda tympani branch is already in connexion with N. mandibularis, as will be described in connexion with N. VII.

N. VI.—The abducens nerve can be well seen on both sides in its peripheral course running forwards from the level of the otic vesicle, internal to the mandibular nerve, to end in the upper and posterior pole of the orbital pre-muscle mass. On both sides the nerve receives numerous radicles from the ventro-lateral border of the hind-brain internal to the otic vesicle and at a level corresponding with the fourth neuromere. At this point and posteriorly the relations become somewhat confused on the right side owing to an unfavourable plane of section. On the left side, although the fibre-bundles are in places exceedingly fine and occasionally disappear in one section to reappear in the next, a clear picture is nevertheless presented, so that the following description applies mainly to that side. The reconstruction of the nerve in fig. A, though necessarily somewhat schematic, is a faithful representation of the main course of the rootlets. A well-marked radicle, constituting the main posterior root of the nerve, arises from the lower part of the side of the brain internal to N. X. and immediately in front of the most anterior root of N. XII. and in series with it. The former is directed forwards, the latter backwards, while the two are separated by a small ascending branch of the vertebral artery. This radicle, at first directed also somewhat laterally, soon turns dorsally in the mesoderm on the side of the brain, and, reaching a level some twenty sections ( $10\mu$ ) higher than its origin, it joins another

bundle of fibres running from above and behind downwards and forwards. This bundle, traced upwards, rises to a high level close to the brain-wall until it reaches a point corresponding with the neural crest and about midway between the dorsal roots of N. IX. and N. X. Here it becomes very small, but before its final disappearance it seems to have a connexion by a fine rootlet with the brain-wall. This cannot, however, be stated with certainty owing to the minuteness of the structures and the unstained condition of the fibres. A short distance below the point where the bundle becomes lost it is joined by another fine fibre-bundle coming from behind and below. The latter bundle can be traced back to an origin from the anterior root of N. XII., and is apparently to be interpreted as a dorsal branch of that nerve. The above dorso-ventrally running nerve, after being joined by the main posterior radicle, runs downwards and forwards, receives a large root from the lower part of the fifth neuromere a short distance caudal to the otic vesicle, and is further joined to the main posterior radicle by a fine loop of connexion. Internal to the otic vesicle the bundle, now a nerve of relatively considerable size, receives two groups of radicles, one opposite its posterior border and the other a short distance farther forward. The abducens is therefore in connexion not only with the fourth neuromere but directly with the fifth and the brain-wall ventral to the sixth, and indirectly with the posterior unsegmented portion of the rhombencephalon through the anterior root of N. XII. The question of the origin of the sixth nerve with regard more especially to its connexion with a given neuromere has been very variously stated by different authors not only for lower vertebrates but also for man. An excellent summary of the whole subject has been recently given by Gräper. In the case of the human embryo most authors (except Broman, who derives it from the third neuromere) agree with Streeter in attributing the main origin of the nerve from the fourth neuromere (see footnote on p. 10). A posterior origin of the nerve is described by Elze (7 mm.), in whose embryo a radicle arises close to and in series with the roots of N. XII., and indeed a series of radicles extending between the abducens and N. XII. has been more than once described in the literature. Bremer, in a more extended study of the aberrant roots of the two latter nerves, finds that in young human embryos it is by no means uncommon to find the gap between the two nerves filled in by a more or less segmental series of rootlets, some being directed not only backwards or forwards in a ventral direction but also laterally and dorsally. In a 10.2-mm. embryo one of these laterally running roots joins a separate bundle of N. IX. For an 11.5-mm. embryo he figures a condition very similar to that found in our case (fig. 4 in his paper). Gräper, working at the more intimate fibre connexions within



the neuromeral area of the rhombencephalon in several lower mammals, chick, etc., finds that in all cases the abducens is strictly confined in origin and point of exit to the fourth neuromere. He describes, however, in a 13-mm. sheep embryo, a bundle arising from between the fourth and fifth neuromeres and running ventrally and backwards to join N. IX. It would seem, therefore, from the foregoing more correct to regard this row of ventral roots, which occurs more or less normally in the young human embryo and bridges over the gap between abducens and N. XII., not as belonging morphologically to N. VI. proper, but as constituting transitory ventral branches of N. IX. and N. X. The fact that these roots are primarily connected with one another and with the nerves immediately in front and behind, and the further fact that they may possess dorsal branches corresponding with the dorsal divisions of the spinal nerves (Bremer), afford an explanation of the arrangement so frequently found. This interpretation is in agreement with the view of Gräper in that it derives the origin of the abducens solely from the fourth neuromere.

N. VII.—The ganglion of the facial nerve is wound spirally around the acoustic ganglion complex, and grooves the latter, lying somewhat internal above, then anteriorly and lower down on its outer aspect. The two cell masses are partly fused but are in part separated by mesodermal cells and, especially below, by the motor root VII. The central fibres of the ganglion (N. intermedius), in company with those of N. VIII., enter the marginal zone opposite the third neuromere, some running directly into the mantle layer of this neuromere, but large numbers taking a horizontal direction backwards and constituting the contribution of this nerve to the tractus solitarius. The motor root, which is small relatively to the size of the ganglion, arises a short distance below the point of entry of the sensory fibres. The trunk of the nerve runs backwards and outwards under the v. capitis lateralis and comes into relation with the first cleft. The connexion here is not in the form of a tubular placode formation, as is the case with the ganglia of IX. and X., but consists of a thick strand of ganglionic cells merging on the one hand with the cells of the ganglion and on the other with the thickened epidermis of the cleft. From the ganglion a short distance distal to this epibranchial organ a short branch is given off which has an independent connexion with that organ and constitutes the nervus epibranchialis described by Futamura in an embryo of 27 to 30 days (fig. 4). As the main trunk sweeps ventrally and caudally into the hyoid arch it drops off from the lower end of the ganglion an anterior branch, the great superficial petrosal nerve (fig. 4), which carries with it for some distance ganglionic cells. This nerve runs at first lateral to the a. carotidis interna, internal to the dorsal expansion of the first

pharyngeal pouch, across the roof of the pouch itself anteriorly, and into the maxillary process lying close to the epithelium of the roof of the mouth cavity (fig. 5). After running a short distance downwards into the maxillary process, it shoots almost horizontally in the sections as a well-marked bundle across the space separating it from the terminal bundles of n. maxillaris, without establishing any traceable connexion. There is as yet no definite accumulation of ganglion cells in this region. The chorda

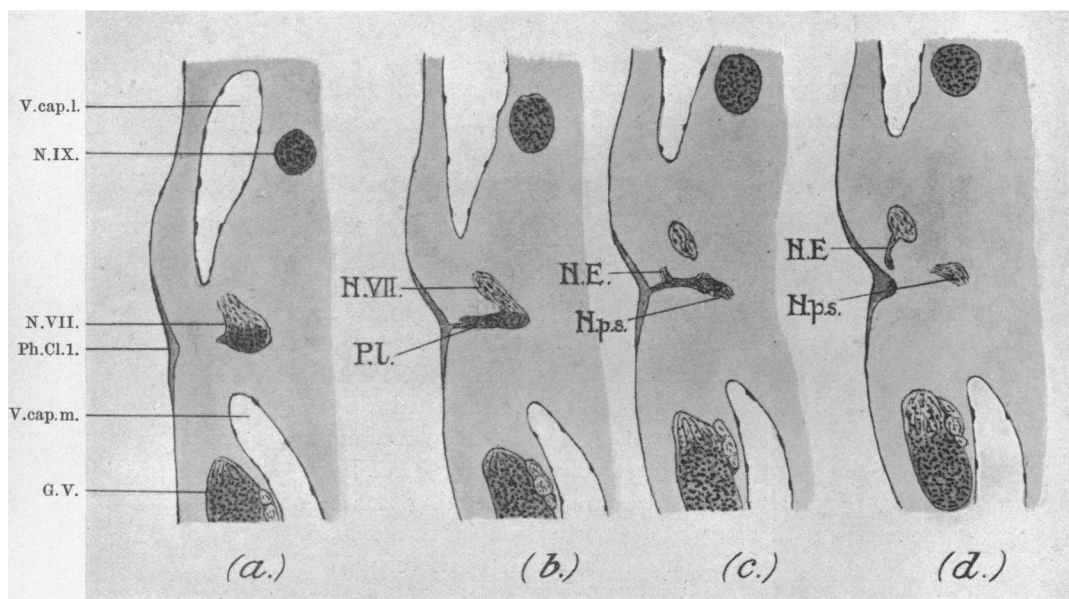


FIG. 4.—Four sections at the level of the placode of N.VII. on the right side.  
(a) Section 229 ; (b) section 232 ; (c) section 234 ; (d) section 336.

tympani is present as a large branch from the trunk of the nerve (fig. 5), running into the mandibular arch in the angle between the epithelium of the first cleft and the endothelium of the first pouch, which meet above it in the cleft membrane. It ends by dividing into two main branches which are directed mesially in the condensed mesoderm of the floor of the mouth, but before this final division it gives off a small branch which curves outwards to connect with n. mandibularis as it runs in the mesodermal Meckelian "gutter" described above. This connexion is not apparent on the right side, although a similar branch is present. The nerve trunk finally terminates in a sharply outlined mass of condensed tissue—the hyoid pre-muscle mass, described by Futamura at this stage.

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The acoustic complex is markedly differentiated histologically in its upper and lower segments; for while the upper portion resembles the adjacent ganglion VII. and the spinal ganglia generally, the cells in the

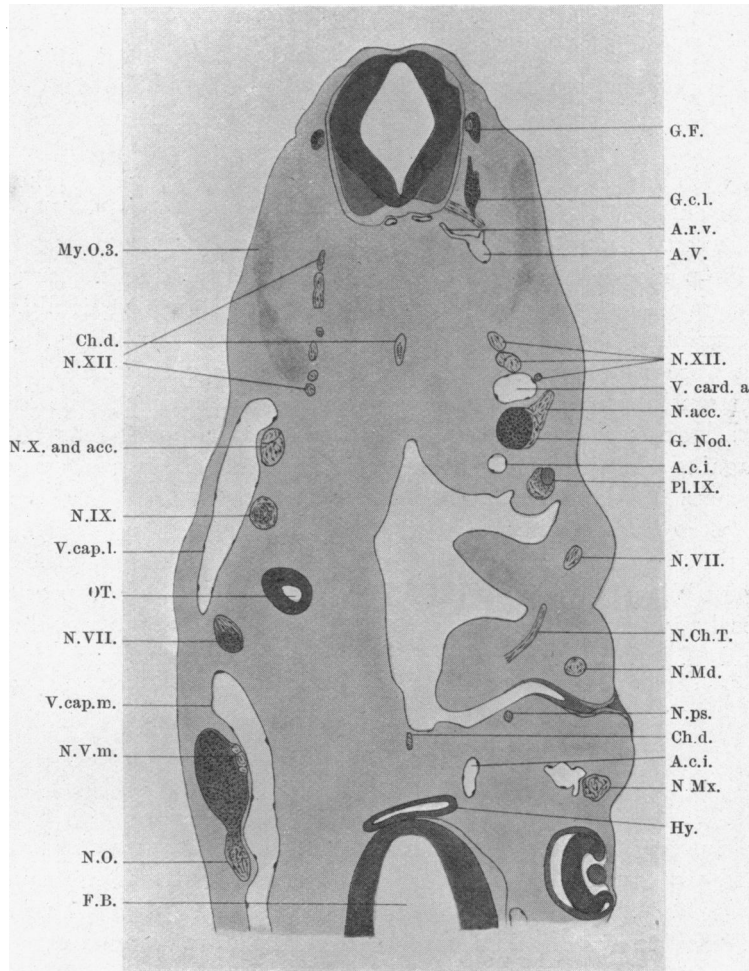


FIG. 5. × 25.

lower portion are smaller, more darkly staining, and more widely spaced. This latter "cochlear" segment overlaps the upper "vestibular" segment especially on its outer side, but also internally, so that the vestibular segment has the appearance of being inserted into it from above. The

cells of this lower cochlear portion further fuse in part with the epithelial wall of the otic vesicle, destroying its sharp outline and leaving no definite line of demarcation between the two structures. Fibres are continued upwards from it internal to the vestibular ganglion, and constitute the young cochlear nerve. The central fibres from the upper part of the ganglion join the marginal zone opposite the third neuromere in company with the fibres from ganglion VII.

N. IX.—The ganglion of Ehrenritter is relatively insignificant, and consists of a small collection of cells almost entirely confined to the lateral aspect of the nerve. Its central fibres join the marginal zone of the hind-brain, some entering the mantle layer of the fifth neuromere, while many turn backwards and upwards, causing a thickening in the "Randschleier" towards the point of entry of the central vagal fibres. The motor root is distinguishable as a small bundle arising a short distance ventrally. The nerve is continued distally internal to the v. capitis lateralis (fig. 5, right side) as a fibro-cellular strand in which the fibres predominate, the cells being apparently all of the "sheath" type. As it approaches the level of the dorsal apex of the second pharyngeal pocket, ganglion cells begin to appear again, and soon the whole cross-section of the nerve consists of a dense mass of darkly staining nuclei forming a large ganglion—the ganglion petrosus. In this structure a definite fibrous (motor) element is indistinguishable as such, in contrast with what has been noted in the case of the ganglion V. and ganglion VII. The ganglion in its lower part comes to be closely applied to the posterior wall of the second pharyngeal pocket (figs. 5 and 6), and here, on the left side, appears a short sprout from its anterior face. This is the only indication of a nervus tympanicus, the presence of which has been noted by Futamura at this stage (27 to 30 days). On the right side is a small but very definite fibro-cellular connexion between the ganglion petrosus and the upper part of the ganglion nodosus. This connexion is absent on the left side. According to Streeter, such a connexion between N. IX. and N. X. is absent in embryos up to 7 mm., and usually also in embryos of that stage, while in slightly older embryos the two nerves come into close relation and may be linked together. Elze in a 7-mm. embryo finds no such connexion, and both His and Streeter figure it at 10.2 mm. Hence in the embryo under description, although the two nerves are still separated by an appreciable interval at the point of connexion, the latter on the evidence must be regarded as of a secondary nature. The nerve trunk, traced down into the third arch, runs lateral to the a. carotidis interna, and gradually becomes free from ganglion cells on its inner aspect, but on its lateral aspect the cells gradually merge into a well-marked placode. The latter consists of a tubular process

of epithelium, opening below on the lateral face of the third visceral arch in the deeper part of the second cleft or "ductus branchialis II." The opening is about  $140\mu$  in diameter from above downward, and from it a finger-like process extends up to the outer side of the distal end of the ganglion (fig. 5), its tip being embedded in the latter structure, so that histologically the two are continuous. A lumen extends through the process for a distance of  $90\mu$  from the mouth of the placode. From this point the nerve curves forwards and downwards to end just lateral to the (medial) thyroid anlage. In this part of its course it is situated some distance anterior to the third aortic arch, but drops off, on the left side, a short internal branch which runs some distance ventrally in close relation to the artery. On the right side (fig. 6) two such branches are present.<sup>1</sup>

N. X. and N. XI.—The development of the vago-accessory complex has been described in detail by Streeter. Nevertheless, a few points come up for special mention, especially as our embryo falls in the gap between the 7-mm. and 10-mm. embryos of his series. The general outline of the developmental stage can be seen in the reconstruction (fig. A). A *vagus* root-ganglion has been definitely differentiated from the neural crest of the hind-brain, its central fibres entering the sixth neuromere (fig. 2). The more posterior part of the crest is represented by four or five ganglionic clumps along the well-developed accessory motor portion of the complex, which clumps gradually diminish in size from before backwards. The accessory nerve is first found at the level of the third cervical segment, from which point it runs cephalad internal to the second cervical ganglion. Almost at the level of the I.C. ganglion, but slightly distal to it, it passes external to a small fibre-bundle coming dorsad and somewhat caudad from this ganglion. It then develops on its outer and ventral aspect a dense ganglionic clump, corresponding in size with the I.C. ganglion itself, but having no connexion with this latter structure or with the hypoglossal rootlets. This aggregation of nerve-cells might be regarded either as a detached portion of the I.C. ganglion, an arrangement which, according to Streeter, frequently occurs; or, on the other hand, it might with quite as much probability be looked upon as a *Froriep* ganglion. Its position some distance caudal to the rootlets of N. XII. is not against this view, for the process which, as Streeter suggests, has brought about the breaking up of the neural crest into clumps, viz. the growth of the intervening fibre-tracts, will obviously produce its greatest effect in the case of the most

<sup>1</sup> In the profile reconstruction N. IX. seems to run in the second arch; this is due to the fact that while the nerves are projected on the mid-sagittal plane, the visceral arches, etc., are represented in *surface* outline, so that the deeper relations, viz. the obliquity of the second cleft, are not shown.

posterior member of the series and thus cause marked caudal displacement. In a 10·2-mm. and in a 14-mm. embryo Streeter figures the ganglion in a position well caudal to the most posterior rootlet of XII. Its shape furthermore corresponds with the general description given for a Froriep ganglion, in that it tapers off anteriorly in contradistinction to the

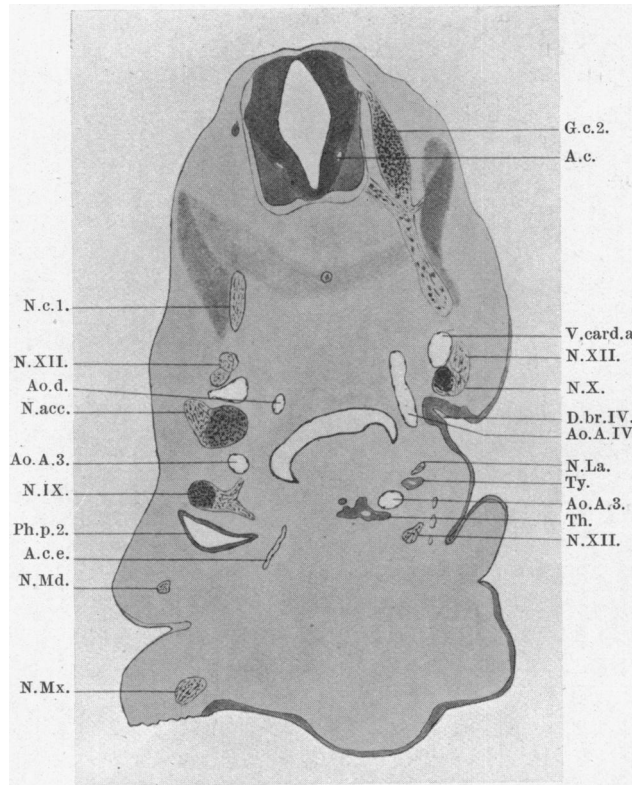


FIG. 6.  $\times 25$ .

accessory cell clumps. There is no well-defined Froriep formation on the right side, where the I.C. ganglion is better developed and extends dorsally to the accessory nerve, sending most but not all of its central fibres internal to this structure. The ganglion jugulare, with the accessory motor root applied to its posterior aspect, is continued down as a fibro-cellular strand, free from ganglion cells, to the ganglion nodosum (figs. 5 and 6). The v. capitis lateralis crosses the trunk of the nerve laterally and then runs behind it. The motor portion leaves the upper part of the ganglion

nodosum and passes dorsally and laterally, crossing the vein, N. XII. and N. I.c., to end in three branches in a condensed mesenchyme,—the anlage of the sterno-cleidomastoid muscles. The lower part of the ganglion lies dorsal to the third and fourth pharyngeal pockets, and opposite the fourth visceral arch it gives off a large branch which curves downwards and inwards in the anterior part of this structure (fig. 6, left side) anterior to the fourth aortic arch, to end dorsal to the ventral aorta close to the hypoglossal nerve. This is the superior laryngeal nerve, and it gives off, as is best seen on the right side, an external branch which runs in the posterior part of the arch external to the artery, and represents in all probability the external branch of the superior laryngeal nerve of the adult. The placode in connexion with N. X. is a short epithelial cul-de-sac continued from the upper end of the fourth visceral cleft. The cells of its tip blend with those of the ganglion at the level of the origin of the superior laryngeal nerve. The vagus trunk then passes caudad lateral to the sixth aortic arch, is crossed by N. XII., and comes to lie in the mesodermal tissue lateral to the œsophagus and trachea (comp. figs. 6 and 7). It can be traced well beyond the tracheal bifurcation (fig. 10), where it breaks up into branches which run to the developing bronchi, and others which form a plexus around the œsophagus containing much syncytial sympathetic tissue, as will be later referred to in connexion with that system. A terminal ramification on the fundus of the stomach cannot be made out.

N. XII. arises by a series of ten or eleven rootlets from a longitudinal thickening of the mantle layer already described as a prolongation of the anterior horn anlage into the hind-brain. The series, individually separated by ascending branches of the vertebral artery, extends from the level of the vago-accessory trunk to within a short distance of the origin of the ventral nerve-root C.I., the anterior rootlet, as has already been noted, having a fine loop connexion with the origin of N. VI. These rootlets unite to form three bundles, which in turn fuse together to form the main hypoglossal trunk. The two fan-like anterior occipital myotomes are in lateral relation to the rootlets, somewhat widely separated above but in contact with them below, where the first myotome sends a wedge of pre-muscle tissue between the two anterior roots. The third occipital myotome lies for the most part caudal to the posterior group but overlaps it. From the most anterior root on the left side a large branch detaches itself, running at first laterally across the back of the anterior cardinal vein and then caudally postero-lateral to this vessel (fig. 5), so that dorsal tributaries of the latter separate the nerve from its parent trunk. This aberrant nerve, which is altogether absent on the right side, rejoins the main trunk of the hypoglossus below. The latter

lies at first behind the ganglion nodosum, separated from it by the anterior cardinal vein. It then winds spirally around these structures, is crossed by the accessory nerve, and turns sharply upwards and medialwards to end near the (median) thyroid anlage (fig. 6). At the lowest point of the bend it drops off a branch which can be followed some distance caudally, dorsal to the pericardium and left auricle, to end in the mesodermal anlage of the

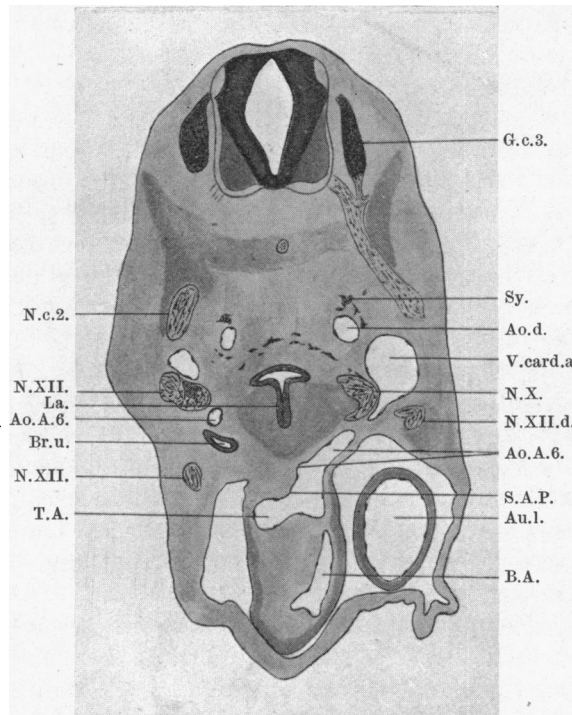


FIG. 7.  $\times 25$ .

infra-hyoid musculature—the descendens hypoglossi (fig. 7, left side). The hypoglossal trunk is joined posteriorly by the first two and part of the third cervical nerves, the arrangement being essentially similar to that described and figured by Elze and Streeter. In one important point, however, the arrangement indicates an advancement on the Elze (7 mm.) embryo, inasmuch as the cervical contributions join the trunk of N. XII. relatively much lower down; in fact, the C. III. fibres connect with the ramus descendens rather than with the main trunk, so that we are here a step nearer an “ansa” formation typical of a 10-mm. stage. From the



proximal end of the nerve trunk and from the distal ends of its constituent roots there extend towards the dorsal aorta cords of typical syncytial sympathetic cells ("cellular rami") similar to those to be later described in connexion with the spinal nerves. Dorsal to the aorta in each section there appears at this level a small collection of syncytial tissue constituting a cephalic prolongation of the sympathetic cord. We are here, therefore, dealing with the anlage of the upper end of the first cervical ganglion, the connecting cords probably representing the early stage of the hypoglossosympathetic connexion of the adult.

*The Spinal Nerves.*—Dorsal roots. The neural crest extends unbroken from ganglion C. II. to within a short distance of the tip of the spinal cord. In the cervical and dorsal region it has undergone almost complete segmentation into ganglia, which, however, remain connected by a cellular bridge. The C. I. ganglion has no connexion with the second on either side. As we go caudal to the lower lumbar region the connecting bridge becomes relatively more important in size than its ventral ganglionic offsets, while still further caudal the ganglia are represented only by the teeth of the serrated ventral border of the crest. In all about thirty-four dorsal spinal ganglia are definitely demarcated on either side. In general they are connected dorsally with the thickened ridge of marginal zone containing the early postero-lateral fibre columns in which the entering dorsal root-fibres assume for the most part a longitudinal arrangement. The distance between ganglion and thickened marginal zone diminishes as we go back, until ultimately, in the lower lumbar region, the dorsal border of the crest comes into direct contact with the postero-lateral ridge through cellular ganglionic processes, containing a few fibres. Still further caudal the dorsal border of the crest rises towards the dorsal aspect of the spinal cord, higher at some points than at others, so that, although there is here no fibrillation, the dorsal border of the crest shows a serration similar to the ventral border. This picture suggests that in the ventral migration of the neural crest some parts lag behind at regular intervals, this process commencing before the dorsal border has reached the level of the future thickened postero-lateral ridge and giving rise to dorsal processes of the crest itself. When these dorsal serrations reach the level of the ridge they become here attached to the spinal cord by fibres which are at first very short, subsequently becoming longer owing to the differential growth of the parts. In other words, it would scarcely seem quite accurate to regard the first dorsal rootlets as a secondary connexion through a sprouting of fibrous processes between two relatively widely separated points. Ventral root-fibres can be definitely noted as far caudal as the first coccygeal segment, the more posterior groups of the series arising from an undifferentiated

neural wall, the more anterior (as far caudal as S. II. segment) from a definite anterior horn anlage. The ganglia are connected with the ventral roots in the cervical and dorsal regions by well-marked fibrous processes in which neurocytes (Kohn) are scattered. In the lower lumbar and more caudal segments the ventral root fibres run through the ventral poles of the ganglia (figs. 20 and 21). This suggests a process similar to that occurring in the dorsal poles of the ganglia, viz. the pole of the ganglion itself comes in the first instance into immediate relation to the ventral root and short fibre connexions are established, gradually becoming longer as growth of the roots and cord takes place. An early dorsal branch of the complete spinal nerve is present from C. II. to C. VI. inclusive on the left side (see fig. 6). These branches are short, directed laterally, and spread out fan-like to enter the inner face of the myotome. There is none in connexion with C. I., and that in the case of C. VI. is very small. On the right side they are not so well seen owing to the slight obliquity of the sections, but there is a well-marked dorsal branch from C. I. on this side. The spinal nerves are connected with one another by anastomoses down to S. II., those between the individual cervical nerves and D. I. being especially large. The anastomotic loops closely invest the ventral aspect of the root of the membranous costal processes. In the dorsal region they are much finer, but that between D. XII. and L. I. shows a definite increase in size, while the individual lumbar nerves and the first two sacral nerves form a thick band of connexion among themselves. The nerves are well advanced on their ventral course in the lateral wall of pericardium and coelom, but show no division into terminal lateral and anterior divisions. The phrenic nerve arises from the anastomoses between C. III., IV., and V. nerves, and runs ventrally and caudally towards the pleuro-pericardial membrane, which it just fails to reach (figs. 9 to 12). It lies at first dorsal to the anterior cardinal sinus; then, hooking around the termination of the subclavian vein, it passes almost horizontally in a ventral direction lateral to the termination of the posterior cardinal vein, and at its termination lies dorso-lateral to the duct of Cuvier (fig. 9). The innervation of the upper extremity is in the form of a plate-like expansion which projects laterally into the root of the limb from the anastomoses between C. V., VI., VII., and VIII., beyond which the individual nerves project ventrally towards the lateral wall of the pericardium without actually reaching it (rami pectorales). This plate is best marked opposite C. VI. and VII. nerves, and divides into two leaves, a dorsal and a ventral, which show a condition of differentiation intermediate between Elze's 7-mm. embryo and his Embryo II. (fig. 452, Keibel and Mall). The dorsal plate, besides its main process (radialis), has nearer its oral edge a short process directed towards the pre-axial

border of the limb. From the ventral leaf of the plate musculo-cutaneous, median, and ulnar processes are distinguishable. The latter, after a short course as a single trunk, divides on both sides into two branches which can be followed some distance distally in close relation to the marginal (brachio-ulnar) vein in the postaxial border of the limb. The nerve and its branches lie anterior and ventral (*i.e.* pre-axial) to the vein. The subclavian artery, as is described in greater detail below, springs from the seventh dorsal segmental artery and pierces the nerve plate between C. VI. and C. VII. nerves. Between the dorsal and ventral leaves it gives off a branch towards the radial nerve, and soon breaks up into two branches, a larger accompanying the median and a smaller accompanying the ulnar nerve. The main vein of the limb (*vide infra*) runs along the postaxial border, then orally dorsal to the dorsal leaf of the nerve plate in its whole extent (fig. 12 *et seq.*), and crosses anterior and ventral to the phrenic nerve to join the cardinal sinus opposite the duct of Cuvier. The basis of the lumbosacral plexus is represented by the strong anastomoses between the lumbar and sacral nerves. This connecting band expands somewhat opposite the hind limb into a slightly differentiated plate which sends processes for a short distance into the root of the limb.

*Sympathetic Nervous System and Anlage of the Suprarenal Cortex.*—A definite chain of sympathetic—or sympatho-chromaffin (Zuckerkandl)—tissue is present from the level of the ganglion nodosum to the level of the umbilical arteries. Further forward in the head region and in connexion with the more anterior cerebral nerves, viz. between the distal extremity of the superficial petrosal nerve and the n. mandibularis, a similar type of tissue is suggested in the form of scattered cells, which cannot however be ascribed with any certainty to the sympathetic system. The nerve bundle, “almost entirely free from ganglion cells,” which Elze (7 mm.) describes as lying medial to the trigeminal ganglion and which he provisionally regarded as of sympathetic nature, corresponds exactly in position and appearance with N. VI. in our embryo, and is doubtless in the former case also a portion of that nerve in its peripheral course. The sympathetic cord has a fixed position throughout, lying at first dorso-lateral to the a. carotis interna, then in a similar relation to the aortic roots and later to the aorta itself. The histological characters of its constituent cells are not absolutely constant, but there is always the frequently occurring mitotic figure, the darkly staining nucleus and protoplasmic body provided with short processes, and with a tendency in common with its neighbours to run together into a syncytium as described by Kohn, Zuckerkandl, and others (Pl. I. fig. 2). In the cervical region there is a commencing ganglion formation, the cord appearing in some sections as a few scattered cells and

in others as a dense clump with a remarkably definite outline. This appearance is less evident in the dorsal and lumbar regions owing to the fact that the cord here gets broken up into a looser network by the insertion of the brush-like ends of the rami communicantes. The first fibrous ramus appears in connexion with N. C. VIII. (fig. 15). More orally the cord is frequently connected with the cervical nerves, and then anastomoses by loose chains of sympathetic cells constituting the "cellular rami" described by Kohn for the rabbit (Pl. I. fig. 2). Such a cellular ramus is present in the case of N. C. I., and, as has already been described, similar chains of cells appear between the ganglion nodosum, the hypoglossal rootlets, and the sympathetic cord at these levels. Fibrous rami are present from C. VIII. to L. III., caudal to which the rami again become cellular. Here, however, in the narrow space between the aorta and the spinal nerves the sympathetic chain becomes closely applied to the latter, so that the term "ramus" can scarcely be employed to describe the connexion. Where a fibrous connexion is present it takes the form of at least two, and in many cases three, distinct bundles from each spinal nerve, the more posterior bundle often fusing with the anterior bundle of the nerve next caudal before it reaches the sympathetic chain (fig. 21). Especially is this the case with the lower dorsal and upper lumbar nerves. The rami spread out into an almost continuous brush on reaching the cellular chain, loosening it up into a network of cells rather than a close syncytium. In the lumbar region, where the cord is more longitudinally cut in the sections, the protoplasmic processes of the cells can be seen to be directed longitudinally within it, but it is questionable whether distinct nerve fibres are present apart from the entering fibres of the rami communicantes. Anlagen of the coeliac, aortic, and hypogastric plexuses are represented by a ventral streaming of fibres and sympathetic cells from the chain as well as directly from the rami. This fibro-cellular migration is most marked around the origins of the coeliac and omphalo-mesenteric arteries (figs. 17, 18, 19), but is present in some degree down to the level of the umbilical arteries. The fibres and cells pass ventrally around the aorta, between it and the Wolffian body, and more orally they are closely applied to the inner face of the anlage of the suprarenal cortex. A fibre connexion of the sympathetic migrations of opposite sides across the anterior aspect of the aorta cannot be made out, but syncytial clumps of sympathetic cells are present in this position, especially around the origin of the coeliac artery. Similar clumps extend into the root of the mesentery of the stomach and intestine. Surrounding the whole length of the oesophagus, and especially on its dorsal aspect, are numerous collections of darkly staining syncytial tissue, undoubtedly sympathetic, in a position similar to that of the "Hals-aorten-

geflecht" figured by His for a fourth-day chick, and constituting a myenteric plexus in combination with numerous small branches of the vagus (fig. 7 *et seq.*) Similar ganglionic collections, but fewer in number, are present at the lower end of the trachea around its bifurcation, also in association with vagal filaments, and represent the anlage of the cardiac plexus.

The anlage of the suprarenal cortex is present in the first five dorsal segments. It is situated between the aorta medially, the mesonephros laterally, and the Wolffian arteries dorsally (fig. 16 *et seq.*). It does not reach the dorsal pillar of the pleuro-pericardial membrane anteriorly as it does in slightly older stages (Zuckermandl). Histologically its component cells are markedly differentiated from the surrounding mesoderm cells, and show an "epithelial" character, the nuclei being larger and more deeply staining and the cells rounder and with a closely aggregated arrangement. Caudally the cell condensation is separated from the coelomic epithelium by a relatively wide area of undifferentiated mesoderm, but orally the relation is more intimate, the intervening mesoderm containing numbers of cells of the above type which connect the anlage with a broad ridge of the coelom between the mesonephros and the root of the mesentery. The mesial face of the anlage has closely applied to it the ventrally streaming sympathetic fibres and cells (figs. 17, 18, and 19). In its substance are numerous small veins (see fig. 18), which can be frequently seen to open into the posterior cardinal sinus as mesial ventral tributaries of this vessel. These latter branches more caudally are concerned in the formation of the subcardinal vein (*vide infra*). Notwithstanding the close relation of the Wolffian arteries to its dorsal surface, no branches of these vessels could be seen entering the anlage.

#### ORGANS OF SPECIAL SENSE.

*The Olfactory Organ.*—The wax model of the nasal organ (Pl. I. fig. 3) falls naturally into the series of models by Peter, figured in his *Atlas der Entwicklung der Nase und des Gaumens*, and resembles his model of a 9.2-mm. embryo. The nasal area is sunken into a pit, looks laterally as well as ventrally, and is surrounded by a well-developed rampart which is best marked on the lateral aspect and here forms the lateral nasal process. Only anteriorly is the boundary wall indistinct, but even here there is an appreciable elevation demarcating the pit from the general surface. The medial nasal process is most prominent posteriorly—processus globularis (Keibel)—and is continued back along the ventral surface of the head some distance beyond the posterior margin of the pit. Here it is bounded on its lateral aspect by a still shallow oblique groove which is continued forwards

to cut into the posterior margin of the pit and backwards and inwards along the future roof of the mouth—the ventral limiting groove of the maxillary process. The external limiting groove of the maxillary process, or naso-lacrimar groove, is continued downwards and forwards from the optic anlage and cuts into the nasal margin a short distance anteriorly and laterally, so that the tip of the maxillary process forms the postero-external boundary of the pit for a short distance, and separates the lateral from the mesial nasal process.

The nasal pit is continued backwards and somewhat inwards as a blind sac for a distance of about  $110\mu$ . The floor of the sac is formed by a thick complete raphe of epithelium, the ventral border of which is attached along the groove which we have termed the ventral limiting groove of the maxillary process, and is continuous with the epithelium covering this process and the medial nasal process. There is no wide groove separating the two processes as in His's figure of a twenty-nine days embryo, the accuracy of which Hochstetter and Keibel have questioned. Such a groove is further absent in Peter's series. A comparison of the model with that by Peter for a 10.5-mm. embryo shows that the ventral limiting groove is much shallower and less marked than in the latter owing to the fact that the two processes are less pronounced. The groove is thus a secondary formation, and in neither case can it be regarded as a gutter connecting the hinder end of the nasal pit with the roof of the stomodæum. In general the appearances confirm the view of an early fusion of the maxillary and medial nasal processes to form the posterior boundary of the nasal pit and the "primitive Gaumen," the fusion taking place from within outwards (Keibel) as the respective processes expand. A bridging over by these two processes of a pre-existing groove connecting the nasal pit with the stomodæum, as described by His, is not compatible with the form of the parts at this early stage. The anlage of the organ of Jacobson is present in its earliest form (fig. 8). It does not appear on the model, but can be observed as a faint grooving of the epithelium of the medial wall of the nasal pit, similar in appearance and position to that figured in the Normaltafel of Keibel and Elze (fig. 32) for an embryo of 8.5 mm. The latter is the earliest in which this anlage has been noted.

*The Eye.*—The development of the eye marks a stage in advance of that of Hochstetter's 7-mm. embryo, described in detail by Elze and reproduced as fig. 169 of Keibel and Mall's *Text-book*. The optic cup is connected with the diencephalon by a short widely-open pedicle. The laminae of the cup are still separated by a wide interval. The outer lamina consists of two or three irregular layers of nuclei and contains traces of pigment. The lamina inversa is greatly thickened and has become differentiated into

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two layers, an outer radial layer of protoplasmic strands and nuclei resembling the radial layer of the neural wall, and an inner fibre layer also radial but cell-free except for a few nuclei scattered in each section. The

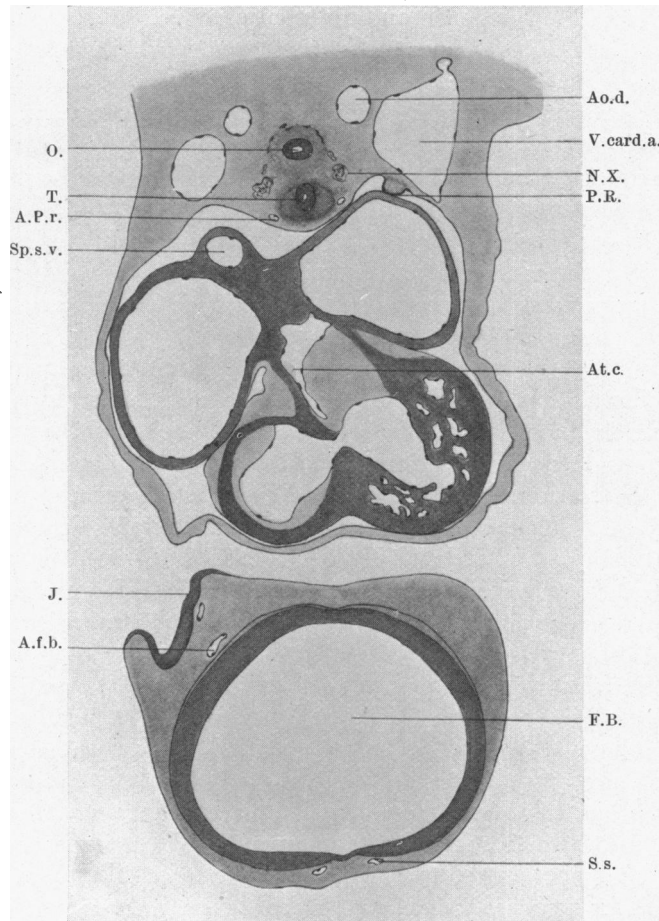


FIG. 8.  $\times 25$ .

edge of the cup (fig. 5) is closely apposed to the surface epithelium dorso-anteriorly (*i.e.* relatively to the long axis of the embryo). Besides the mesodermal cells surrounding the blood-vessels and those flowing over the edges of the cup, the antrum cupulæ contains scattered cells which may have been derived from these latter sources, or, as pointed out by Lieberkuhn, from the migrating (?) cells of the otherwise cell-free inner zone of the

lamina inversa. The chorioid fissure is open along its whole length, but the distal ends of the fissure come very close together on the right side.

The lens vesicle is quite closed, its external contour being complete. Its cavity contains degenerating cells lying free and partly clumped together. Its posterior wall is thickened and differentiated into an outer cellular and an inner radial cell-free layer indicating a commencing fibre formation. It is still in contact with the surface epithelium on both sides. In general it has a circular outline in the sections, but has the appearance of being compressed between the lamina inversa retinae and the surface. This is probably due in part at least to the manipulation of fixing and embedding. At the level of contact with the surface epithelium the lens anlage has a flattened pear-shaped outline, the narrower end of the pear causing a protrusion of the surface. The surface epithelium is one-layered over the point of closure in a few sections of the left side, and consists of cubical cells; elsewhere on this side and entirely on the right it is two-layered. The epithelial layers, however, undergo a modification in two respects in the immediate neighbourhood of the point of closure: mitotic figures become more frequent in both layers, and the nuclei of the outer layer lose their typical flattened form and assume the round form seen in the cubical cells of the stratum germinativum. It is not definitely ascertainable whether the single layer above referred to, and which Elze describes for both sides of the 7-mm. embryo, is to be regarded as a continuation of the outer or the inner layer. The impression suggested by a study of the modification of the surrounding epithelium is that it rather represents *both* layers. In other words, the process of closure might be regarded as consisting of a primary growing over of one layer, viz. the superficial layer (Elze), followed later by the other layer; or we might, with greater probability, premise a resolution of the two-layered epithelium into its primary one-layered form at its "growing-point." When the closure has been effected by the active growing over of this single layer, the latter then differentiates once more into its two layers.

The a. hyaloidea is represented by a large sinus-like blood space lying in the anterior part of the chorioid fissure, projecting into the antrum cupulae and coming into contact with the lens vesicle. It is connected distally with a capillary plexus around the edge of the optic cup, and proximally with a capillary system lying along the pedicle; and through this apparently with the capillary vessels of the maxillary process. An arterial branch, to be later referred to, springs from the a. carotis interna over the optic stalk (a. ophthalmica), but there is no connexion present between this vessel and the anlage of the a. hyaloidea except an indirect one through the capillary plexus on the outer face of the optic cup.



*The Ear.*—The anlage of the labyrinth lies lateral to the fourth neuromere of the hind-brain. The ductus endolymphaticus (fig. 2) is about  $500\mu$  in length on the left side, and on the right  $700\mu$ , the disparity in length being probably largely apparent and due to the obliquity of the plane of section. It opens into the otic vesicle proper on its medial aspect about  $130\mu$  below the tip of the latter. In its upper half it shows a roughly triangular outline on cross-section, the epithelium at the anterior and posterior angles being markedly thickened, forming sharp ridges on its external aspect. This occurs to a less extent at the outer angle. In its lower half the angles become rounded off and the outline oval. The tip and most of the outer wall consist of a single layer of epithelium, the inner wall, like the rest of the labyrinthine anlage, being 2 to 3 cells thick. In the otic vesicle itself a lower, more tubular cochlear segment can be distinguished from an upper vestibular portion, in which the anlagen of the anterior and posterior semicircular canals are indicated by a pouching of the wall. A bulging of the lateral wall somewhat lower down suggests a commencing external canal. The lower end of the vesicle is widely separated from the first pharyngeal pouch, which lies ventrally and laterally. In the intervening mesoderm runs the a. carotis interna with the dorsal root of the incomplete second aortic arch. In the primitive tympanic cavity there is an anterior and posterior tympanic recess separated by a groove, the groove for the tensor tympani, corresponding with Hammar's model of an 8-mm. embryo (fig. p. 274 of Keibel and Mall's *Text-book*). From the anterior tympanic recess a short groove is continued downwards and forwards on the roof of the pharynx. The relation of the n. chorda tympani to the tympanic cavity has been already referred to in connexion with that nerve.

#### THE ALIMENTARY CANAL AND ITS DERIVATIVES.

On the floor of the pharynx are present the tuberculum impar, with immediately lateral to it on either side a swelling, situated on the ventral end of the first visceral arch. The copula is well marked, and is continuous back into high arytenoid folds. The hypophysis has a wide connexion with the roof of the pharynx, and is closely applied to the floor of the diencephalon (fig. 5). It is flattened dorso-ventrally and shows a slit-like lumen. Near its distal extremity ends the chorda dorsalis, from which it is separated only by a small interval. Its apex is bifurcated and is continued into two short solid horns.

The first pharyngeal pouch presents nothing for description further than has been mentioned under the primitive tympanic cavity. The second epidermal cleft runs very obliquely forwards as well as in a medial direction, and is continued into a well-marked ductus branchialis II. (Rabl)

into which, as has already been noted, opens the placode in connexion with N. IX. The third pharyngeal pouch is much smaller than the two preceding, and has a short dorsal and a long ventral process, the lumen throughout being reduced to a mere slit (Pl. I. fig. 4) by the thickness of its walls. Its closing membrane is situated at the bottom of the sinus cervicalis. The pouch is connected with the pharynx by a still widely open ductus pharyngo-branchialis III. The differentiation of the anlagen of the epithelial bodies and thymus is well advanced, and agrees with the descriptions of Groschuff, Kohn, and Maximow. The ventral prolongation of the pouch—or thymic anlage proper—is continued ventrally and medially, at first dorso-posterior to the third aortic arch, to end close to the thyroid anlage (fig. 6) on the lateral aspect of the truncus arteriosus. Its wall consists of several layers of densely packed cells, the posterior wall being thicker than the anterior. This thickening is continued on to the posterior and dorsal wall of the pouch itself. The anterior and outer walls of the latter have quite a different histological structure. Pl. I. fig. 4 is a drawing of a horizontal section through a portion of the pouch. A lumen is practically non-existent. The posterior wall shows the close arrangement of the nuclei in the thymic thickening, while the loose arrangement in the anterior wall offers a marked contrast. Here the smaller but more darkly staining nuclei are studded through a pale (chromophobe) vacuolated protoplasmic syncytium in an irregular manner. This portion of the wall of the pouch constitutes the anlage of the “epithelial body III.” (Kohn) or parathyroid.

The “caudal pharyngeal pouch complex”—to use the term suggested by Grosser—consists of a relatively involuted fourth pouch with short dorsal and ventral pockets. The anterior wall of the pouch and the outer wall of the ventral pocket show the same histological differentiation as has been above described for the epithelial body III., and constitute the anlage of the epithelial body IV. There is no definite “thymic” thickening present as in the case of the third pouch. There appears further in connexion with this pouch a comparatively long ventro-caudal tubular process at first sight similar to that of the third pouch, but a closer examination of the sections shows that the resemblance is merely superficial. The process under consideration is not a direct continuation of the ventral pocket, which is itself small, but it arises more dorsally and laterally from the body of the pouch. Furthermore, a distinction is indicated by its relation to the aortic arches; for whereas the ventral prolongation of the third pouch is in close dorso-posterior relation to the third arch, the structure in question is separated by a wide interval from the fourth arch and is in close antero-ventral relation to the sixth arch (fig. 7). This arrangement suggests the

former presence and later disappearance of such a vessel as Elze (7 mm.) describes as running "close to the ventral wall of the postbranchial body," namely, the rudimentary fifth aortic arch, which vessel in our embryo is represented only at its extreme dorsal end. The structure under description is to be regarded, therefore, as the derivative of a fifth pouch or "ultimobranchial body" of Tandler. Its ventral extremity approaches the pericardium closely (fig. 7), and lies about  $300\mu$  caudal and lateral to the thyroid anlage.

The thyroid anlage, as shown in fig. 6, is bilobed, with a dorsal and a lateral sprout from each lobe. A lumen is present in the proximal part of the left lobe. The component cells, of which the nuclei are large, round, and darkly staining, are closely packed together and show a commencing column formation. The distal end of the thyro-glossal duct can be followed proximally through nine or ten sections ( $10\mu$ ) as a solid epithelial cord. The anlage as a whole lies in the apex of the V formed by the third aortic arches overlapping these vessels and the bifurcation of the truncus arteriosus.

*The Larynx and Lungs.*—The arytenoid folds are well developed. The lumen of the laryngeal cleft is to a large extent obliterated by a fusion of its walls (fig. 7), but orally a small lumen remains, while posteriorly there is a slit-like communication between œsophagus and trachea. The lumen of the trachea, at first merely a cleft like that of the larynx, soon broadens into an oval, and later presents a circular appearance. Further caudally its form varies in cross-section from a circle to an oval, with the long axis either lateral or antero-posterior. The bifurcation occurs in the sixth cervical segment. The condition of differentiation of the pulmonary sacs, as ascertained from an antero-posterior graphic reconstruction, shows an advance on Narath's figure for a 7-mm. embryo (fig. 342, Keibel and Mall), and on Elze's model (*ca.* 7 mm.) (*cf.* figs. 10-13 and 15). The left stem bronchus has a large lateral bud directed somewhat dorsally (fig. 11)—the "first ventral bud" of Aeby, or "lateral" bud of His—and ends in a swollen but undifferentiated flask-shaped extremity. From the right stem bronchus spring an apical or eparterial bronchus (fig. 12) and a first ventral bronchus bud (fig. 13), the latter of which is somewhat constricted at its origin. Immediately caudal to the origin of the ventral bronchus on this side, the stem bronchus, as can be seen in fig. 13, shows an expansion in a dorsal direction, indicating the formation of a dorsal bronchus bud at this point. The mesodermal lung anlage shows a corresponding lobing on its outer surface. The relation of the pulmonary artery to the primary bronchi and their branches is described below (*cf.* Pulmonary Artery).

The œsophagus is at first crescentic in outline, with the concavity

directed ventrally; lower down it becomes either circular or elliptical. The wall consists of three or four layers of nuclei grouped for the most part in the middle thickness, leaving an outer basal layer free from nuclei, and an inner layer with few nuclei but with relatively numerous mitotic figures. The epithelial tube is surrounded and closely invested by con-

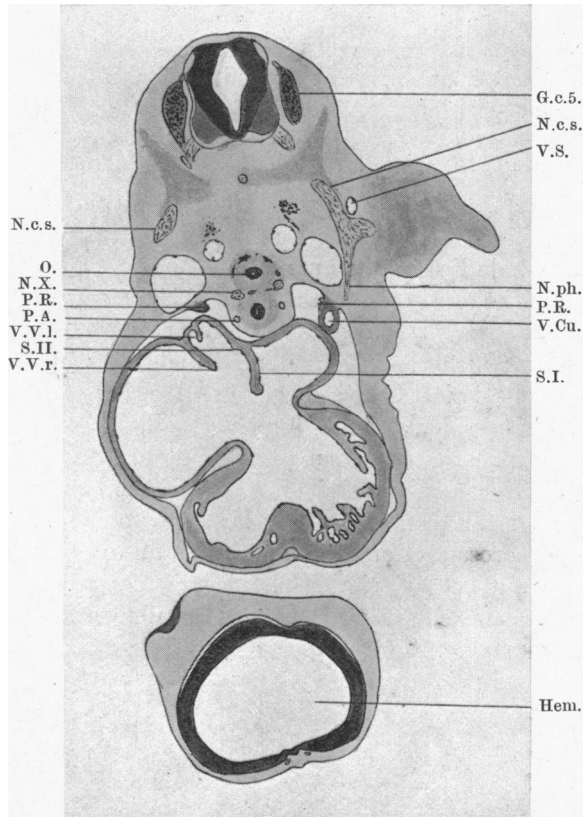


FIG. 9.  $\times 20$ .

denser mesenchyme with large nuclei, many of which are spindle-shaped, arranged concentrically in layers. This mesenchymal condensation is best marked below at the level of the bifurcation of the trachea, being absent at its upper end, and constitutes the circular cesophageal pre-muscle mass. It is covered externally by a continuous nerve-plexus layer, already described as composed of small masses of sympathetic tissue and branches from both vagus nerves (figs. 7-10).

The torsion of the stomach is not yet complete (*cf.* figs. 13, 15, 16, and 17). The widely expanded fundus is blown out to the left, and the organ as a whole is arched out well to the left of the plane of the middle line, while the pylorus and beginning of the duodenum are situated in that plane. The concentric "pre-muscle" arrangement of the investing mesoderm, seen in the lower end of the oesophagus, ceases at the cardia. In the root of the mesentery in this region are clumps of syncytial sympathetic tissue, and similar but smaller ganglionic masses are scattered dorsal to and to the right of the cardiac end of the stomach. No connexions with the sympathetic or vagal fibres are to be observed. The

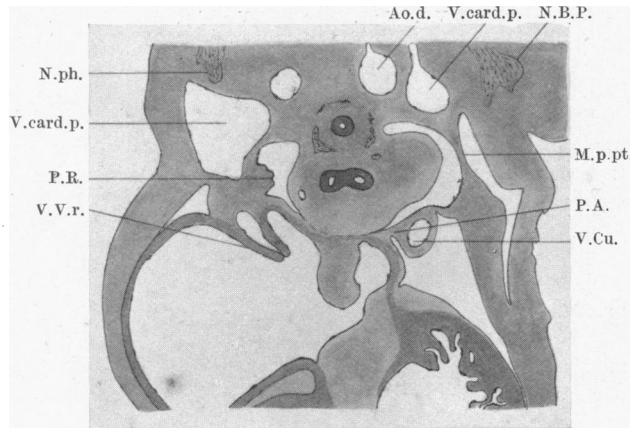


FIG. 10.  $\times 25$ .

blood-vessels of the stomach are represented by the a. gastrica sinistra, the splenic plexus (*cf.* below), and the small vein which runs from the fundus through the lesser omentum to join the ductus Arantii.

The duodenum has a patent lumen throughout. The intestinal tube from the pylorus to the apex of the intestinal loop runs somewhat to the right of the plane of the middle line (fig. 19). The intestinal loop has undergone a torsion of about  $110^\circ$ , so that the distal limb lies well oral in respect to the proximal limb (figs. A and 19). The apex is situated in a funnel-shaped pouch of the coelom in the base of the umbilical cord. A short distance proximal to this point the already slender intestinal tube becomes still further reduced in diameter, less sharply defined against the surrounding mesoderm, and loses its lumen through four sections (in position marked + in fig. A). The vitello-intestinal duct has separated, but remains of that structure appear in three distinct places in the sections,

in each case through a few sections only, as a slender column of degenerating cells lying free in the coelom of the cord and surrounded by an aggregation of blood cells representing the extravasated blood of the omphalo-mesenteric artery (*cf.* fig. 17). The distal limb of the loop increases greatly in diameter from the apex to a short distance beyond the cæcum, beyond which it narrows again and is continued caudally in the middle line as large intestine and rectum. The connexion between the latter and the rest of the cloaca—"cloacal duct" of Reichel—is narrowed dorso-ventrally by an extensive development of the urorectal septum (figs. A and 20), and laterally by low broad vertical ridges of

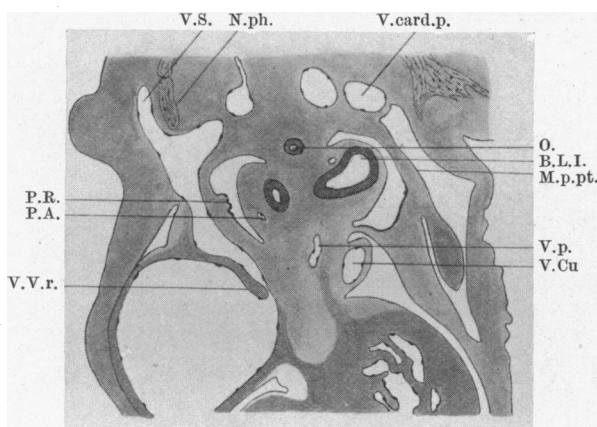


FIG. 11.  $\times 25$ .

mesoderm continued down from the lateral parts of the septum and swelling towards each other from either side. The duct is further constricted below by a transverse ridge from the inner face of the cloacal membrane, and has a dorso-ventral diameter of  $130\mu$ . A caudal intestine is present as a small blind finger-like pouch opening into the aboral part of the rectal cloaca and continued back as a solid cord of endothelial cells through nine sections ( $10\mu$ ). Further caudally and in line with this column a small interrupted epithelial "rest" appears (fig. A). The allantois comes off the anterior pole of the cloaca at a sharp angle, as is seen in fig. A, the transition from the latter organ to the former being a sudden one and not a gradual merging of one into the other (fig. 20). At first the allantois consists of a tube of small calibre which enters the root of the body-stalk and gradually insinuates itself between the umbilical arteries (figs. 20, 19, and 17). In this position it soon expands into a dorso-ventrally flattened

vesicle (fig. 17), and later, still increasing in calibre, it assumes a roughly circular outline in cross-section. In the distal part of the cord it branches so that in several sections a group of two, three, or more allantoic vesicles is to be seen. The allantois is lined throughout by a single layer of cells: at its origin from the cloaca and in its early tubular portion in the base of the body-stalk the cells are cubical, with pale protoplasmic cell bodies and rounded nuclei; more distally, where the tube expands and becomes vesicular, the cells become flattened and drawn out and the structure as a whole less sharply demarcated against the surrounding mesoderm.

#### LIVER, PANCREAS, SPLEEN, AND CÆCUM.

The entodermal liver tissue extends on the left side as the left coronary appendage dorsally and orally as far as the ventral pillar of the pleuro-

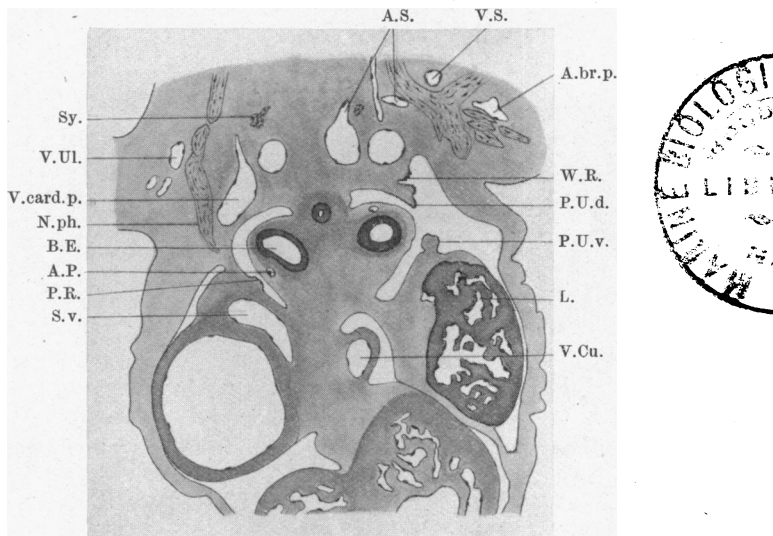


FIG. 12. × 25.

peritoneal membrane, in the substance of the "pericardio-peritoneal membrane" (fig. 12). From the latter structure it bulges laterally into the antero-lateral recess and appears anteriorly in a few sections in a fold which is attached to the lateral aspect of the pleuro-peritoneal membrane (fig. 11). Caudo-ventrally it lies embedded in the substance of the mesoderm of the dorsal pericardial wall (septum transversum) and bulges into the peritoneal cavity, coming almost into contact with the lateral abdominal wall. Further ventrally, having joined the right lobe, it reaches and fuses

with the anterior abdominal wall caudal to the pericardium (compare figs. 12, 13, 15, and 16). Posteriorly the left lobe appears as a wing-like expansion of the right lobe (fig. 16), demarcated from the latter ventrally by the groove for the left umbilical vein, which here runs in the middle line to join the ductus Arantii. The right lobe, though exceeding the left in bulk, does not extend so far dorsally and orally; its coronary appendage is less marked and fails to reach the pleuro-peritoneal membrane (fig. 13). It extends, however, much further caudally,<sup>1</sup> frees itself from the dorsal

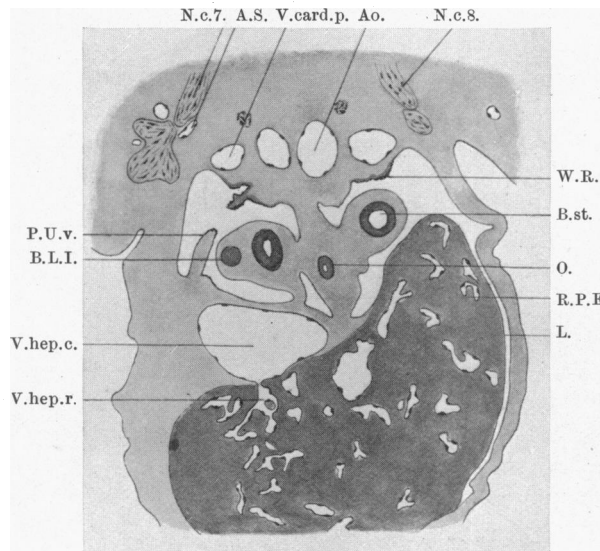


FIG. 13.  $\times 25$ .

mesentery, and bounds orally and ventrally the peritoneal cleft which connects the bursa omentalis with the greater peritoneal cavity—the hiatus communis recessuum or future foramen epiploicum (*cf.* fig. 17 and below). The gall-bladder (Plate II. fig. 5) lies in a deep wide groove of the liver, filled with dense mesenchyme which separates it from the liver substance. Proximally the cystic duct becomes free from the liver, the mesoderm surrounding it causing a slight swelling under the peritoneum, and just before its junction with the hepatic duct a lumen appears within it. At this point the hepatic duct itself also acquires a lumen which is partially double. The common duct contains a lumen in its whole extent, and near

<sup>1</sup> Making every allowance and correction for the obliquity of the sectional plane, which has been done throughout.



its junction with the duodenum gives off the ventral pancreas anlage (Plate II. fig. 5, and fig. 18). The common duct at its origin from the duodenum is at first directed dorsally, to the right and orally. After giving off the ventral pancreas it twists on itself and runs orally ventrally and to the right, the cystic duct continuing this direction, while the hepatic duct takes an almost directly oral course (Plate II. fig. 5). The latter continues orally ventral to the omphalo-mesenteric vein (fig. 17) and soon becomes embedded in the liver, where its outline against the liver tissue proper becomes in many sections irregular and indistinct, the appearances suggesting the giving off of liver trabeculæ. It can be traced, however, some distance in the substance of the liver as an irregular column of cells, smaller, darker, and more densely packed than the surrounding liver cells, until finally it loses its identity by merging gradually into normal liver tissue. The cells of the liver trabeculæ consist of large polyhedral cells with dense granular protoplasm fitting close together and containing a large round, more lightly staining nucleus with usually two or three dark nucleoli. The endothelium of the numerous blood spaces closely invests the trabeculæ, so that a perivascular space is seldom apparent. Typical "blood-forming" cells are absent, although a certain number of darkly staining cells, with little protoplasm and much smaller than the normal liver cell, occur scattered through the trabeculæ and show a general resemblance to ordinary mesoderm cells. A few occur singly immediately beneath the endothelium.

*Pancreas.*—A wax model has been prepared of the dorsal and ventral pancreas anlagen, the hepatic ducts and a portion of the left lobe of the liver and omphalo-mesenteric vein. A drawing of the model is reproduced in Plate II. fig. 5. The ventral pancreas anlage is in the form of a lobulated sessile knob attached to the common bile duct close to its origin from the duodenum. The lobules contain wide-open longitudinally running lumina (fig. 18), with a general arrangement of one central lumen with a lateral lumen on either side. The central lumen opens into the bile duct, and its major portion is situated caudal to this communication. In the case of the lateral lumina no direct connexion either with the central lumen or with the bile duct could be made out, but the histological picture presented by the endothelial walls suggests an opening in both cases into the central lumen at its junction with the bile duct. Owing to the torsion of the proximal portion of the bile duct around the duodenum the ventral pancreas is directed dorsally and somewhat to the right and abuts against the vena omphalo-mesenterica, the wall of which it indents (fig. 18). It is separated from the proximal portion of the dorsal anlage only by a small interval. The dorsal pancreas springs from the duodenum

dorsally and to the left side immediately proximal to the entrance of the bile duct. It is lobulated like the ventral pancreas and is much larger, and lies in the dorsal mesogastrium with its long axis almost dorsoventral. The vena omphalo-mesenterica, in its spiral course dorsally and orally around the left aspect of the intestinal tube, is in close relation to the anlage grooving it on its right side and caudal face (Plate II. fig. 5, and fig. 18). In the latter position the groove is especially deep, owing mainly to the fact that a process of pancreatic tissue is continued caudally in the interval between the vein and the duodenum, lying close against the former (fig. 18). This process is separated from the duodenum by a deep notch. The anlage contains irregular lumina throughout, including the above-mentioned caudal process, in which one of the lumina is relatively large. The proximal portion of the lumen, or common duct, enters the duodenum in an obliquely oral direction, so that the latter appears in this position to have a double lumen through a few sections.

*Spleen.*—The anlage of the spleen is represented by a thickening of the coelomic epithelium over a relatively large area of the dorsal and lateral aspects of the left leaf of the dorsal mesogastrium, with proliferation of its elements (figs. 17 and 18). The thickening is best marked at the level of the origin of the dorsal pancreas, and results in the production of an epithelium several layers thick and consisting of a somewhat chromophobe protoplasm in which numbers of small round nuclei are set. It is demarcated from the underlying mesoderm by a layer of this lightly staining protoplasm with few nuclei. The area of the mesogastrium corresponding with the epithelial thickening projects from the surface and, where the proliferation is best marked, is notched on its coelomic aspect. The underlying mesoderm, which shows no special differentiation except for the presence of numerous mitotic figures, contains a plexus of blood-vessels which is connected on the one hand with the omphalo-mesenteric vein caudal to the dorsal pancreas, and on the other with the left gastric branch of the coeliac artery (*vide infra*).

*The Cecal Region.*—Fig. 6 on Plate II. is a drawing of a wax model of the apex and major portion of the intestinal loop, with a part of the superior mesenteric artery. On the distal limb of the loop a short distance from the apex is an ampullary swelling. From the lateral aspect of the ampulla springs a hollow diverticulum in the form of a short blunt cone directed orally and laterally. The diverticulum shows no distinction into basal and apical portions except in so far as its lumen may be divided into an ampullary section and a diverticular section proper. The ileum and colon are not quite in the same straight line, the latter being displaced somewhat laterally at its commencement relative to the former. This

relation of these two portions of the tube can be observed from the outer aspect, but is better marked as regards the lumen, so that the arrangement is best described thus:—the lumen of the colon followed orally divides as into the two limbs of a **Y**, one limb being continued into the ileum, the other ending blindly at the apex of the diverticulum. At the junction of the limbs of the **Y** the lumen undergoes enlargement. The ileum is thus inserted obliquely into the tube formed by the appendix and colon taken together. Immediately proximal to the appendix is a second smaller and solid epithelial appendage of the intestinal tube (Plate II. fig. 6). It has a similar direction as the former structure, *i.e.* orally along the ileum and laterally, and, though possessing no lumen, its cells, especially in its basal portion, are arranged regularly around a potential central cleft. Proximally it is partially embedded in the wall of the ileum, while its base winds round to the oral and dorsal aspect of the intestinal tube. The exact nature of this decidedly abnormal structure is not apparent. Its position with respect to the apex of the intestinal loop on the one hand, and the appendix on the other, would seem to rule out the possibility of its being a Meckel diverticulum, but it must be remembered that our knowledge of the growth relations of the various organs is very incomplete. The lack of accurate observations in this direction, and especially in the case of the alimentary canal, has been recently emphasised by the work of von Berenberg-Gossler, who proves conclusively that the whole of the rectum and colon as far as the cæcum must arise from the cloaca. In the present case the only safe criterion—namely, the relation of the structure to associated blood-vessels—is impossible of application, so that the question is incapable of definite solution. Another possible interpretation of the abnormality is that it is of the nature of those intestinal diverticula which have been described in the literature as occurring not only in the neighbourhood of the hepatic outgrowth but along the whole length of the ileum, and which have been generally regarded as pancreatic in nature. In this connexion it is interesting to note the observation of Wright, who finds an accessory pancreas in Meckel's diverticulum near the umbilicus.

#### HEART AND BLOOD-VESSELS.

The sinus venosus receives the two ducts of Cuvier and the v. hepatica revehens communis. Its slit-like opening into the atrium is bounded by two well-developed venous valves. The left valve passes below towards the left to end near the distal extremity of the dorsal prolongation of septum I. Orally it fuses with the right venous valve to form the venous septum (septum spurium). A few sections cephalad from the point of fusion of the two valves a septum detaches itself from the left aspect of

the venous septum near its base, and, rapidly increasing in height, passes obliquely over the posterior wall of the spatium septo-valvulare to end near the small septum II. This part of its course is marked on the outer surface of the heart by a distinct groove (fig. 9). This septum would seem to be a continuation of the left valve, as though the latter had again parted company with the venous septum, but that it is in reality of such a nature cannot be definitely stated owing to the complete fusion of the two valves immediately below. Septum I. is well developed (fig. 9), its

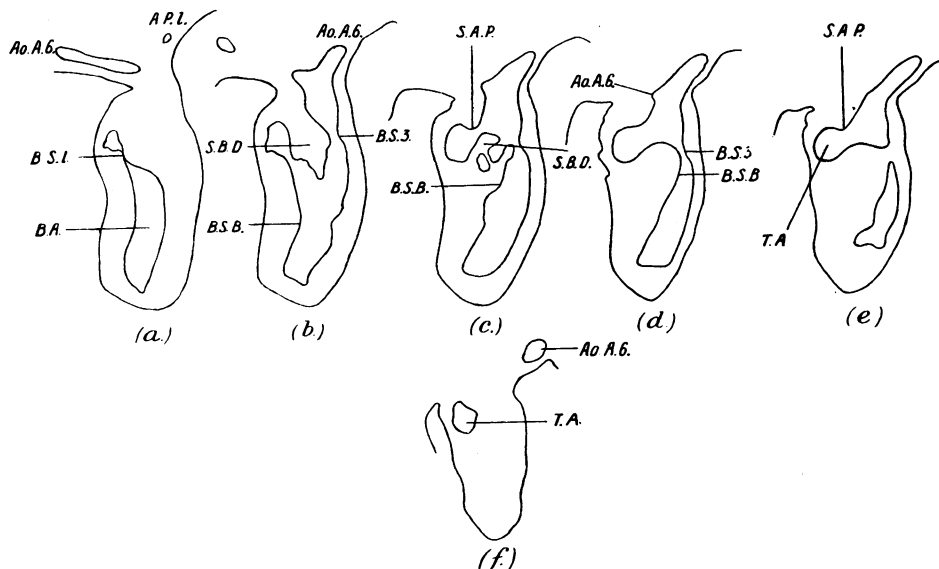


FIG. 14.—Tracings of six sections through the bulbus arteriosus. (a) Section 333; (b) section 329; (c) section 325; (d) section 321; (e) section 318; (f) section 313.  $\times 25$ .

free border being thickened and covered by a thickened endocardium. Its dorsal and ventral prolongations can scarcely be said to actually reach the endocardial cushions of the auricular canal; the dorsal one approaches its associated cushion very closely, but the ventral horn fades away into the ventral wall of the atrium before reaching the ventral cushion. The attached base of the septum shows two small perforations—an early foramen ovale II. A commencing septum II. is present as a short low ridge of myocardium to the right of the upper part of septum I. (fig. 9). The interventricular septum is still low. In the bulbus arteriosus proximal and distal bulbar swellings are well marked, and by their union with one another have brought about a partial separation of the bulbus into truncus aorticus and truncus pulmonalis. In fig. 14 are reproduced

tracings of six sections at various levels through the bulbus which exhibit the main features of the process at this stage. The proximal bulbar swellings A and B (Tandler) have the classical arrangement, the former beginning on the anterior wall of the bulbar portion of the ventricle and running distally on to the posterior wall of the bulbus, the latter passing from the posterior wall proximally to the anterior wall distally. Of the distal bulbar swellings described by Tandler in his model of the bulbus of the embryo  $H_6$ , and numbered 1 to 4, two, viz. 1 and 3, can be identified in the sections, and have produced the distal bulbar septum by uniting across the bulbar lumen, dividing it at this point into pulmonary and aortic constituents. The bulbar swelling A reaches the distal bulbar swelling 1 (fig. 14*a*), while swelling B fuses with swelling 3—that is, with the anterior pillar of the distal bulbar septum. Further, a blunt wedge of mesoderm juts into the bulbar lumen from an oral and dorsal aspect, so that both sixth aortic arches arise by a short common stem (figs. 7 and 14). This structure, the septum aortico-pulmonale, reaches the distal bulbar septum only through its dorsal and ventral prolongations, leaving between the edges of the two septa a foramen of communication between the aortic and pulmonary trunci.

Three complete aortic arches are present (fig. B). A pulmonary artery arises on each side from the sixth arch near its ventral origin. Each lies at first ventro-lateral to the trachea, passing dorsally later, the left before the right. The latter vessel runs caudally ventral to the apical (eparterial) bronchus bud (*vide* Lung, and fig. 12) and then dorsal to the first ventral bud, as His has shown for a 10·5-mm. human embryo, and Flint for the pig. The left artery passes back dorsal to the first ventral bud of the right side, and both arteries end by breaking up into a capillary plexus on the dorsal aspect of the flask-shaped extremity of the stem bronchus.

Into the lateral aspect of the dorsal extremity of the sixth arch on the left side opens a very small vessel, which can, however, be followed through a few sections. This stump is in the position of the original dorsal termination of the fifth arch, and corresponds with the findings of various observers, viz. Elze in a 7-mm. embryo. There can be little doubt that this structure represents the extreme phase of the involution of this vessel.

The truncus arteriosus bifurcates anteriorly into the third aortic arches. From the commencement of the third arch on either side a small vessel runs forwards beneath the pharynx—the external carotid. It becomes lost at the level of the first cleft and cannot be followed into the first visceral arch. The only definite branch which it gives off is one passing outwards and downwards as the second arch—the *a. lingualis*. There is, however, also in the arch a short upwardly directed vessel which might

perhaps be regarded as the ventral end of the second aortic arch. From the dorsal extremity of the third arch the dorsal aorta passes forward as the internal carotid artery. Immediately behind the level of the otic vesicle it gives off a comparatively large branch which is directed back-

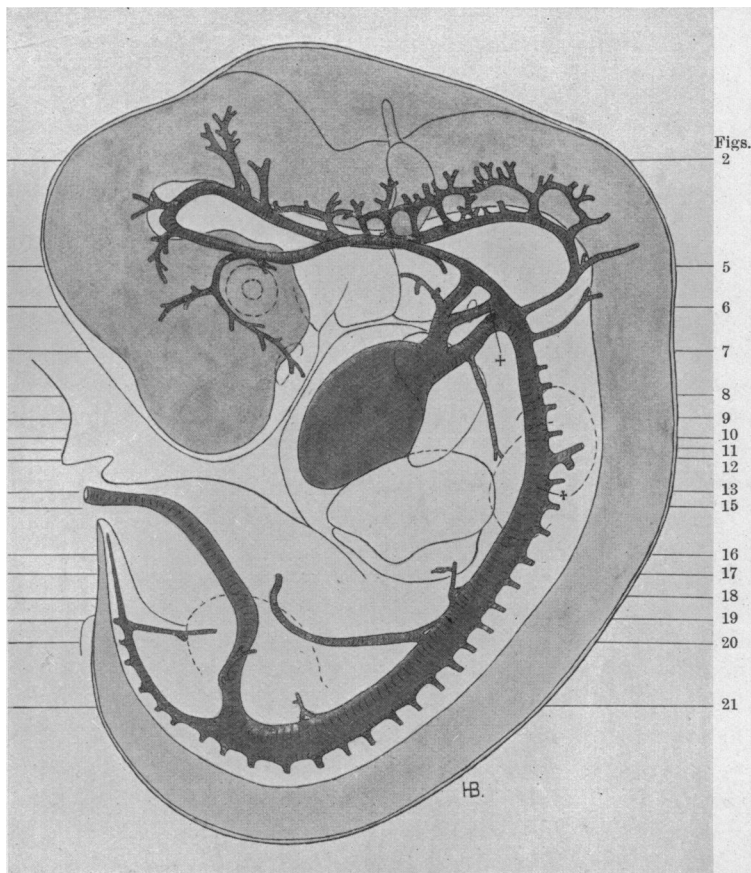


FIG. B.  $\times 12\frac{1}{2}$ .

wards and downwards into the second visceral arch. On the right side this vessel terminates by dividing into two branches, both directed ventrally. This vessel must be identified as the dorsal part of the second arch, or, after Tandler, the root of the stapedia artery. The a. carotis arches past the hypophysis, and as it passes over the optic cup it gives off a small ophthalmic branch. This vessel on the left side soon divides into two

branches, one of which can be traced to a capillary plexus on the upper pole of the retinal anlage. On the right side, where the artery is in a less contracted condition and the plane of section at the same time more favourable, the ophthalmic artery can be seen to pass out laterally over the optic cup and to connect with a plexus surrounding the edge of the cup and especially its temporal rim. This plexus is connected below with the anlage of the a. hyaloidea through a relatively large branch which passes out through the distal end of the chorioid fissure (*vide* Eye). The a. hyaloidea itself is represented by a large sinus-like and plexiform vessel lying in the anterior part of the chorioid fissure and projecting into the antrum cupulæ so as to abut against the lens vesicle. Traced proximally, the artery, besides connecting with a capillary plexus lying along the caudo-temporal aspect of the pedicle, is found to give off a short, stout branch which passes dorsally around the caudo-temporal aspect of the pedicle at the "insertion" of the latter into the cup. It is questionable whether this vessel represents the true proximal continuation of the a. hyaloidea or, as would seem more probable from the observations of Dedekind, Versari, and Fuchs on later stages, the a. ciliaris nasalis. The connexion of the a. hyaloidea with the ophthalmic branch of the a. carotis is thus a very indirect one. A similar independence of this artery is noted by Dedekind (6 mm.) and by Elze (7 mm.), and the condition receives an explanation in the findings of Fuchs in the rabbit, in which mammal he derives the a. hyaloidea from a marginal vessel encircling the edge of the optic cup.

After giving off the ophthalmic artery, the carotid—to follow the interpretation of de Vriese—divides into an anterior and a posterior branch. The former sweeps round the optic anlage, giving off to the side of the fore-brain the anterior chorioidal artery, as described by Mall for 9 mm., and continuing ventrally internal to the nasal pit it breaks up into a capillary plexus over the ventral surface of the fore-brain. Through the plexus there is probably an anastomosis between the arteries of either side. As the artery passes internal to the olfactory epithelium it gives it a branch (fig. 8) seen on both sides. The posterior terminal branch of the carotid curves dorsally and backwards beneath the mid-brain and unites with its fellow (in position marked + in fig. B) to form the a. basilaris, but before doing so it gives off two strong branches to the floor and sides of the mid-brain. The latter together constitute the posterior cerebral group (Mall).

The arteria vertebralis cervicalis arises as the first cervical dorsal segmental artery opposite the dorsal extremity of the sixth aortic arch. It gives branches to the medullary tube identical with those of the

segmental arteries generally (*vide infra*), but continues forward ventrolateral to the hind-brain to unite with its fellow (in position  $\times$  in fig. B) to form the basilar artery. From the vertebral and basilar arteries numerous strong twigs ascend on the side wall of the hind-brain, many passing between the individual rootlets of N. XII. The most marked member of the series supplies the area immediately behind the isthmus, *i.e.* the cerebellar region. These vessels are united with one another by an irregular longitudinal anastomosis.

The roots of the dorsal aorta unite at the level of the 8th cervical segment (fig. B, +). At the level of the 5th lumbar segment, after giving off the aa. umbilicales, it is continued as the caudal aorta to the caudal tip. In several parts of its course the latter appears as two vessels of varying relative calibre, and at more than one level assumes a plexiform arrangement with "Inselbildung," so that the aorta appears at these points in the sections as three or more small vessels grouped together. Even where a single vessel is present it often shows strands of mesoderm traversing its lumen, so that we have here a well-marked instance of "several paths being used by the arterial blood before the reduction to a single vessel" (Evans).

Thirty-two dorsal segmental arteries are present, viz. twenty-five from the aorta proper and seven from the caudal aorta. Distally to the last of the caudal segmentals a few fine capillary vessels are directed dorsally towards the neural tube. In the more anterior members of the series all the principal branches of supply to the spinal cord have been laid down. Each artery runs through the mesodermal intervertebral foramen in company with the vein and anterior to the corresponding nerve, and at the level of the junction of anterior and posterior spinal nerve roots divides into three main branches: (*a*) towards the mid-ventral line of the cord—the a. radicularis ventralis (figs. 5 and 15); (*b*) a branch passing between the dorsal ganglia and the wall of the neural tube and extending as far dorsally as the point of entry of the dorsal roots—the a. radicularis dorsalis (fig. 15); and (*c*) a branch directed laterally towards the myotome. The a. radicularis ventralis when it reaches the lateral edge of the Bodenplatte penetrates the substance of the tube, as the a. centralis, and passes dorsally between the differentiating anterior horn anlage and the undifferentiated radial layer (*vide* Spinal Cord), helping to demarcate the two areas (fig. 3). Between the individual aa. rad. vent. as they turn into the spinal cord a longitudinal anastomosis forms the primitive anterior spinal artery. The a. radicularis dorsalis can in many cases be seen to give a branch into the neural tube at the level of the dorsal extremity of the anterior horn. The branch (*c*) is present only in the case of the most anterior members of the series, viz. the first segmental on the right side, which sends a large vessel laterally



against the myotome. From the latter small branches are continued through the myotome accompanied by venous vessels, while to the outer side of the myotome numerous fine capillaries appear. We may thus speak of a penetrating "ramus cutaneus dorsalis medialis" (Evans).<sup>1</sup> There is no traceable longitudinal anastomosis between the cervical dorsal segmen-

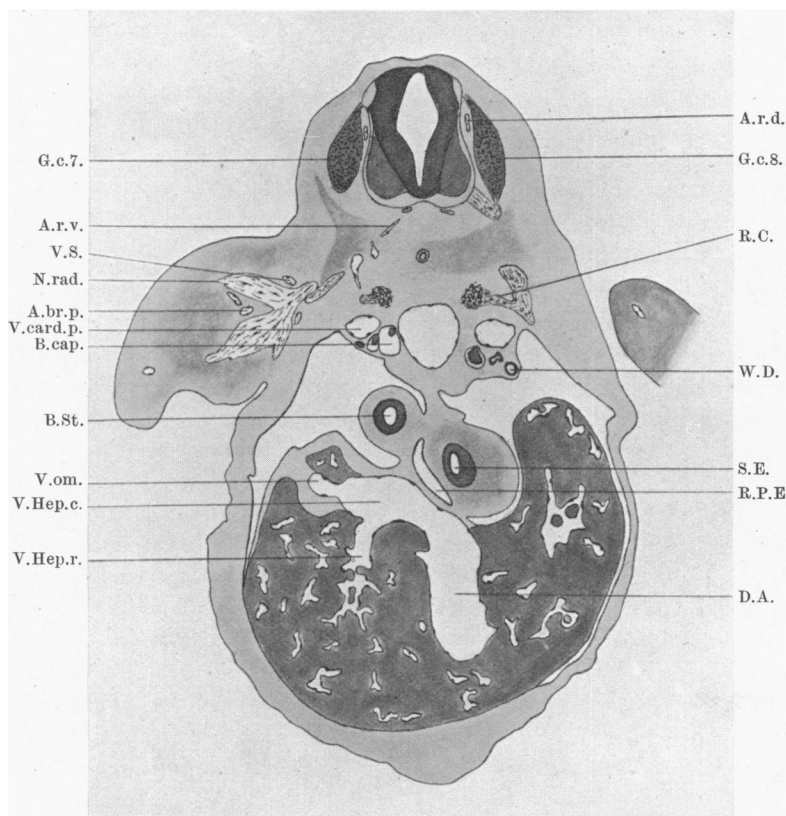


FIG. 15. × 25.

tals to indicate a cervical vertebral system. The first three arteries, however, show a remarkable diminution in their lumina as they approach the aorta, so that at their origins they are little more than capillary in size. As we go caudally the proximal portions of these vessels increase in importance, and this fact, taken in conjunction with the well-developed condi-

<sup>1</sup> The a. rad. dorsalis from the 1st right dorsal segmental passes dorsally *external* to the ganglion, an arrangement which appears quite exceptional.

tion of the spinal branches of the most anterior members, must be regarded as indicating an involution of the aortic roots of these latter vessels.

*Ventral Branches of the Aorta.*—The celiac artery springs from the aorta by two roots opposite the 5th thoracic dorsal segmental. From the loop between the two roots a small vessel passes ventrally and orally into the left leaf of the dorsal mesogastrium—a gastrica sinistra—and connects at the level of the pylorus with a relatively large plexiform vessel lying in the mesoderm beneath the splenic anlage—a. lienalis (fig. 17). This plexus, as has already been mentioned (*vide* Spleen), drains into the v. omphalo-mesenterica caudal to the dorsal pancreas (fig. 18).

The superior mesenteric artery arises opposite the 7th and 8th thoracic dorsal segmentals by a smaller anterior and a larger posterior root. It runs into the mesentery to the left of the intestinal tube and between the two limbs of the intestinal loop towards the caudally directed (originally right) face of the mesentery (Plate II. fig. 6, and figs. 19 and 20). It then passes towards the right across the caudal aspect of the proximal limb of the loop. As it reaches the surface of the mesentery it still possesses a relatively large calibre, but at this point the wall of the artery has been torn in the narrow interval between the mesentery and the lateral coelomic epithelium of the cord so that it cannot be followed distal to this point as a distinct vessel. There is, however, a continuous "clot" of blood cells traceable through about sixty sections and contained in a gutter of parietal coelom without any definite wall (fig. 17). That this collection of cells can be identified as the extra-embryonic portion of the artery is more than doubtful, and it is more probable that it is the result of a tearing of the vessel and an outpouring of its blood as the result of interference with the cord before fixing. It is, however, significant that the remains of the vitello-intestinal duct is found among these cells. The inferior mesenteric artery is small, and arises opposite the 2nd lumbar dorsal segmental by two main roots somewhat confused by "Inselbildung." It runs through about fifteen sections ( $10\mu$ ) before becoming lost in a capillary plexus. It gives a Wolffian branch to the mesonephros (*vide infra*).

The umbilical arteries arise in the 5th lumbar segment and encircle the posterior end of the coelom lateral to the Wolffian duct as the latter runs in the caudal end of the Wolffian mesentery. A short distance from its origin (fig. B) each artery gives off from its posterior aspect the a. ischiadica, which possesses a smaller and a larger root and runs distally and laterally between the teeth of the serrated edge of the hind-limb nerve-plate to break up into a large indefinite plexus. The two aa. umbilicales then approach each other at the root of the body stalk, the allantois inserting itself gradually between them (figs. 20, 19, and 17), a position which it

maintains in its course through the cord. Near the distal end of the latter the two arteries anastomose and after a short course as a single vessel separate again into two. The lumen of each artery is larger in the distal than the proximal part of its course.

From the ventral aspect of the caudal aorta between the last two dorsal segmentals a comparatively large branch runs on either side of the cloaca, just proximal to the cloacal membrane, and into the area oral and ventral to the urogenital section of the cloaca, *i.e.* in the angle between it and the allantois (figs. A and B). This area is drained by a venous plexus forming an anastomosis between the two umbilical veins (*cf.*). Elze describes this arterial branch in an embryo of 7 mm. (*circa*) as running "zur lateralen Seite des Enddarmes an dessen Übergang in die Kloake," but fails to find it in embryos of 9.5 mm. and 11 mm. The vessel in question would therefore appear to undergo rapid development and equally rapid involution.

*Wolffian Arteries.*—On the left side eighteen Wolffian arteries spring from the lateral aspect of the aorta; on the right side nineteen arteries come from the same source and one from the inferior mesenteric artery. They arise irregularly and show no segmental arrangement, the 6th and 7th on the left side for instance arising by a short common stem, while many, particularly in the case of the more caudal members of the series, divide in their distal course into two and supply adjacent glomeruli (fig. 21). The most anterior artery on the right side shows no apparent lumen, appearing merely as a cord of cells, while the second has a definite lumen only at its entrance into the glomerulus. The appearances provided by these arteries are probably associated with the degeneration of the corresponding Wolffian tubules, which cannot, however, be definitely diagnosed in the tubules themselves. As it enters the glomerulus each Wolffian artery shows a localised increase in calibre. The more anterior vessels are in very close relation to the dorsal aspect of the anlage of the suprarenal cortex.

The subclavian artery arches dorsally and laterally from its origin from the 7th dorsal segmental artery.<sup>1</sup> It perforates the base of the nerve-plate between C. VI. and C. VII. nerves without previously giving off any branches. Appearing between the dorsal and ventral leaves of the plate, it continues for some distance as a definitely single large vessel on the dorso-lateral aspect of the ventral leaf—the "a. brachialis profunda" of Erik Müller (figs. 12 and 15). It gives off a branch which is directed along the radial nerve and rapidly becomes plexiform. The profunda trunk itself then shows island formation without the production of a definite

<sup>1</sup> The system of reckoning the dorsal segmental arteries here employed is that of Mall, Tandler, Broman, and Evans. Hochstetter, for instance, describes the arteria subclavia as arising from the *sixth* dorsal segmental. See footnote, p. 605 of Keibel and Mall's *Text-book*.

plexus, the lumen of the vessel being crossed by strands of mesoderm, while numerous short sprouts are given off from it. The vessel then divides into two, one branch continuing along the median nerve, the other along the ulnar, and each remaining as a single trunk for a short distance before appearing in the form of a plexus. The former is the larger of the two and constitutes the main continuation of the arterial trunk. Before penetrating the brachial plexus the subclavian artery gives off a branch which remains on the medial aspect of the ventral nerve-plate and shows a plexiform arrangement at its origin. From the latter point this vessel sends a small but definite branch medially and ventrally towards the pleura (internal mammary?), and continues ventro-caudally as a single trunk—"a. brachialis superficialis" of Müller—medial to the ventral nerve-plate and rami pectorales (fig. 15, right side), to end by turning laterally around the caudal edge of the plate to join the artery accompanying the ulnar nerve. On the left side a complete anastomosis between these two vessels cannot be traced owing to the fact that the artery accompanying the ulnar nerve is smaller on this side than on the right and breaks up earlier into a capillary plexus. Furthermore, the picture is somewhat obscured at this point by small folds in the root of the limb. The a. brachialis superficialis gives off in the same position on both sides, *i.e.* opposite C. VII. nerve, a small branch which pierces the base of the nerve-plate in a dorsal direction. On the left side this vessel ends beside the subclavian vein on the dorsal aspect of the plate.

*The Veins* (fig. C).—The anterior cardinal sinus begins anterior to the Gasserian ganglion as the v. capitis medialis, and is formed by the flowing together of two venous plexuses, one draining the side of the fore-brain and lying dorsal to the optic anlage, the other gathering its radicles from the mid-brain and isthmus region. According to Mall, these two plexuses together constitute the anterior cerebral vein. Both plexuses reach the mid-dorsal line, and form here a more or less definite longitudinal system. Especially is this the case dorsal to the cerebral vesicles, where a fine venous vessel is present on either side of the middle line—the sinus sagittalis (fig. 8). More posteriorly the arrangement becomes less regular. Receiving several smaller tributaries, the v. capitis passes back internal to ganglion N. V. and here receives a large branch from the maxillary arch beneath the optic cup. The latter before its junction with the main trunk is joined by a vein coming from the hypophysis. Closely applied to the lateral surface of the ganglion is a capillary venous plexus in connexion anteriorly and posteriorly with the v. capitis, providing a basis for the later-formed external venous ring. Immediately caudal to the ganglion the vein—now the v. capitis lateralis—gets a double tributary from the

anterior part of the hind-brain (middle cerebral vein, Mall), from which point it runs caudally external to N. VII. and N. VIII., the otic vesicle and N. IX. getting small branches from the first and second visceral arches on its course. Between N. IX and N. X. the posterior cerebral vein enters it

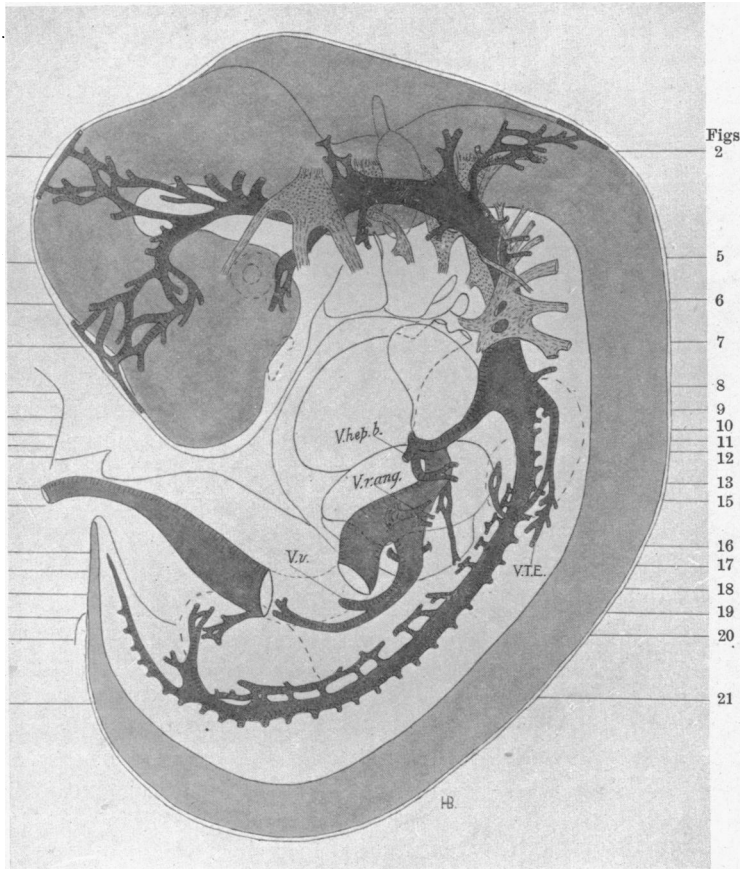


FIG. C.  $\times 12\frac{1}{2}$ .

in the form of a large vessel from the posterior part of the hind-brain, and immediately posteriorly is a smaller branch belonging to the same system. The v. cardinalis anterior then sweeps round the vago-accessory trunk altogether lateral to it, but quickly getting on to its dorsal aspect and separating it from N. XII. It is crossed laterally by the accessory nerve, and lower down by the hypoglossus trunk and its cervical contributions.

Here the vein becomes much increased in calibre and comes to lie once more lateral to the vagus. A large venous plexus lying in the floor of the mouth drains back across the ventral ends of the visceral arches towards the lateral aspect of the vagus trunk—the linguo-facial vein (Lewis). No definite connexion with the v. cardinalis anterior could be made out on either side. As the latter lies dorsal to the auricle it gives off in the 5th cervical segment the duct of Cuvier, relatively longer with a smaller diameter on the left side, shorter and wider on the right. This vessel immediately enters the pleuro-pericardial membrane and sweeps ventro-laterally to enter the lateral horn of the sinus venosus (figs. 9–12). In the latter part of its course the v. cardinalis anterior receives several dorsal segmental tributaries. Opposite the duct of Cuvier, *i.e.* in the 5th cervical segment, it is joined by a large vein which drains the post-axial border of the limb, its tip, and the distal part of its pre-axial border—the brachio-ulnar trunk. As the primitive ulnar vein enters the body-wall from the post-axial part of the root of the limb it is joined by a vein which drains, through superficial tributaries, the lateral wall of the thorax caudal to the arm-bud—the thoraco-epigastric vein of Lewis. The trunk thus formed runs oralwards as the subclavian vein dorsal to the nerve-plate of the limb plexus (figs. 9, 12, 13, 15), hooks around the anterior end of the latter and the phrenic nerve, and is joined before its termination by a small vein from the proximal part of the pre-axial border of the limb.

The posterior cardinal sinus is formed at the level of the 1st sacral segment by the junction of the ischiadic vein from the post-axial border of the hind-limb bud and the relatively small caudal vein from the tip of the tail. The caudal veins remain separate (figs. 20 and 21), but are connected with each other through anastomoses in front of the caudal aorta. From this level the posterior cardinal vein runs oralwards, passing lateral to the origin of the umbilical artery and dorsal to the mesonephros, and receives the dorsal segmental veins. The subcardinal system, the extent of which is indicated in the reconstruction reproduced as fig. C, is present in a well-developed condition. The v. cardinalis posterior as it runs dorsal to the Wolffian body receives two sets of tributaries, a mesial and a lateral. The former are the larger and are best marked in the lower dorsal and lumbar segments, where they anastomose to form a definite longitudinal vessel, lying internal to the Wolffian body and on a plane well ventral to the posterior cardinal—the (medial) subcardinal vein (fig. 19). At the hinder end of the mesonephros this vein is in connexion with its parent posterior cardinal trunk by a large anastomotic vessel (fig. 21), present on both sides, similar to that modelled by Félix in a 9.5-mm. embryo (fig. 574, Keibel and Mall), and forming in his description the posterior termination of the

medial subcardinal. The latter vein is, however, in the embryo under description, continued caudally to this anastomosis internal to the umbilical artery at its origin and dorsal to the mesenchyme of the metanephros to join the posterior cardinal vein just oral to the junction of ischiadic and caudal veins. There are thus two definite channels by which the blood coming from the posterior end of the body can enter the subcardinal vein. In the upper dorsal segments the mesial Wolffian tributaries do not anastomose to form a longitudinal vessel, though many of them are T-shaped as described by Félix. The more anterior members of the series run through the anlage of the suprarenal cortex and take over the drainage of this structure (fig. 18). This anterior disconnected portion of the subcardinal system is further related on the right side to the posterior extremity of the developing anlage of the inferior vena cava, to be later described. The lateral Wolffian tributaries drain dorsally between the individual collecting tubules of the mesonephros. They also unite to form a lateral anastomosing vessel, which, however, fades away behind. The medial and lateral vessels are united together by anastomoses, which can be seen passing between every two Bowman capsules, an arrangement which suggests a functioning mesonephric portal system at this stage. The subcardinal veins of either side have no connexion with each other across the front of the aorta. Of the *venæ umbilicales* the left is very large, and entering the body-wall from the umbilical cord, it receives, besides superficial tributaries from the body-wall, a larger vein coming from a caudal direction. This vein is present also on the right side, and both commence in a plexus which forms an anastomosis between the two and lies in the angle between the antero-ventral surface of the cloaca and the allantois. This vein therefore drains the area supplied by the cloacal branch of the caudal artery, which has already been described in connexion with the latter vessel. Striking the anterior surface of the liver, it grooves the ventral surface of that organ for some distance (fig. 16) before joining with the *v. omphalo-mesenterica* ventro-lateral to the stomach. Before its termination it gives off a large *vena advehens* to the left lobe of the liver—*ramus angularis* (Mall)—and a smaller one to the right lobe. The *vena umbilicalis dextra* has reached an advanced stage of involution and has no longer an independent existence, opening at both ends into the left vein, viz. in the umbilical cord and again immediately before the left vein strikes the liver (fig. 17). Like the latter vein it receives numerous tributaries from the body-wall.

The peripheral portion of the degenerated vitelline vein is present as a blind stump projecting freely into the coelom ventral to the mesentery, and provided with a coating of mesoderm (fig. 19). Entering the mesentery it

encircles the intestinal tube on the left side, and as it winds round to get on to the dorsal surface of the latter it is joined at this point (*i.e.* in the position of the original dorsal or middle vitelline anastomosis) by the superior mesenteric vein (fig. 5, Plate II.). The latter begins in a few small radicles near the tip of the intestinal loop and runs in the mesentery, keeping on a plane to the left of the small intestine and duodenum.

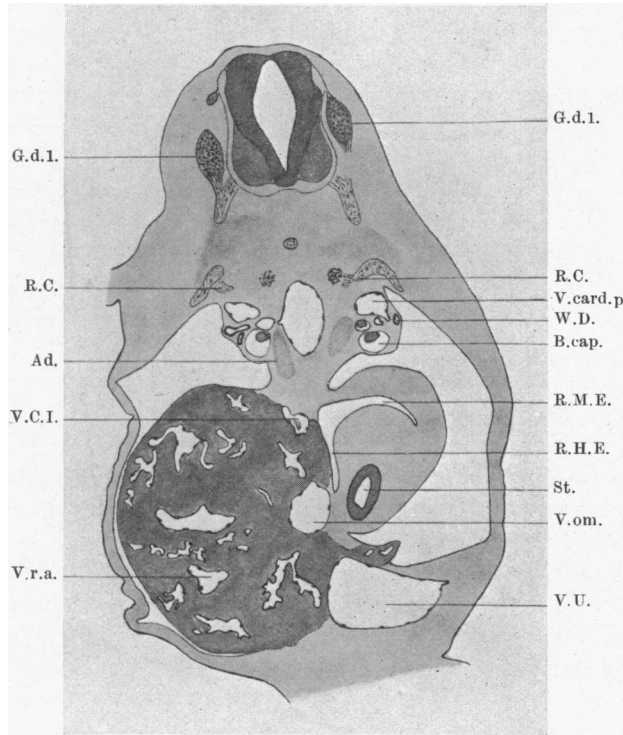


FIG. 16.  $\times 25$ .

The omphalo-mesenteric vein formed by the junction of the vitelline remnant and the superior mesenteric vein winds on to the dorsal aspect of the duodenum, grooves the under surface and mesial aspect of the dorsal pancreas anlage, and applies itself so closely to the now dorsally directed pancreas that its wall is indented by that structure (fig. 18). Continuing its spiral course, the vein plunges obliquely into the left face of the right lobe of the liver to the right of the stomach (Plate II. fig. 5), and joins the v. umbilicalis sinistra. Before its junction with the latter vein it gives off



into the right lobe of the liver a large vena advehens which immediately divides into two, one branch being directed ventrally—ramus arcuatus venæ portæ (figs. 17, 16)—and the other dorsally and constituting the

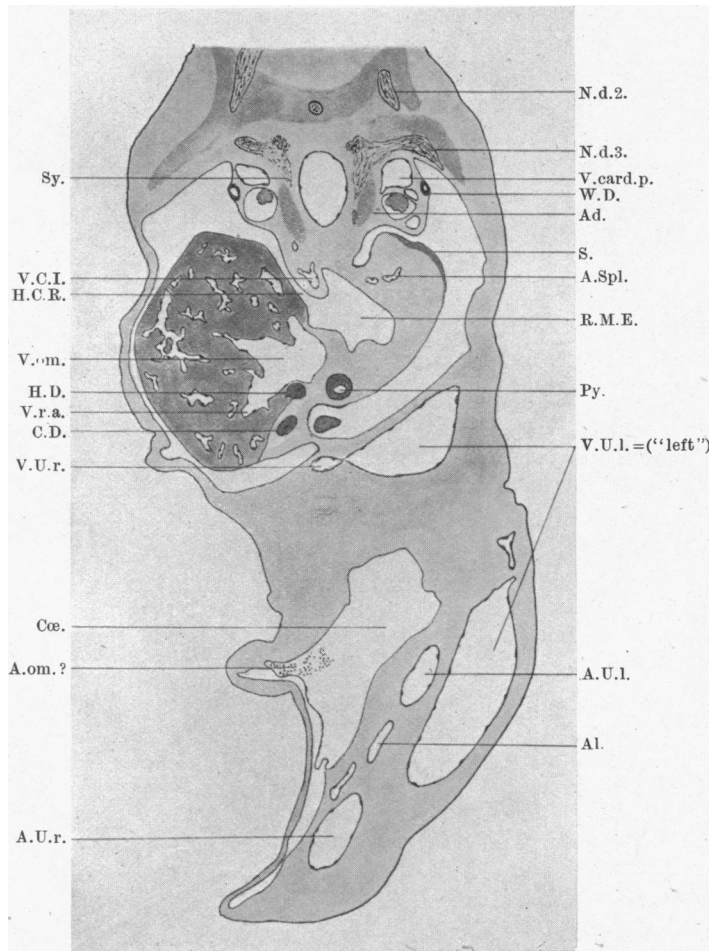


FIG. 17. ×25.

continuation of the main omphalo-mesenteric trunk or right vitelline vein (Mall). From the junction of the v. umbilicalis sinistra and v. omphalo-mesenterica the wide ductus Arantii runs orally and dorsally through the liver (fig. 15), receiving at least one small tributary from the fundus of the stomach through the lesser omentum, as Broman described, to open into the

v. hepatica revehens communis or caudal prolongation of the sinus venosus from the left side. This latter receives also the common opening of the rami dextra and sinistra venæ hepaticæ on its anterior aspect and to the right of the opening of the ductus Arantii, and on its right side the persist-

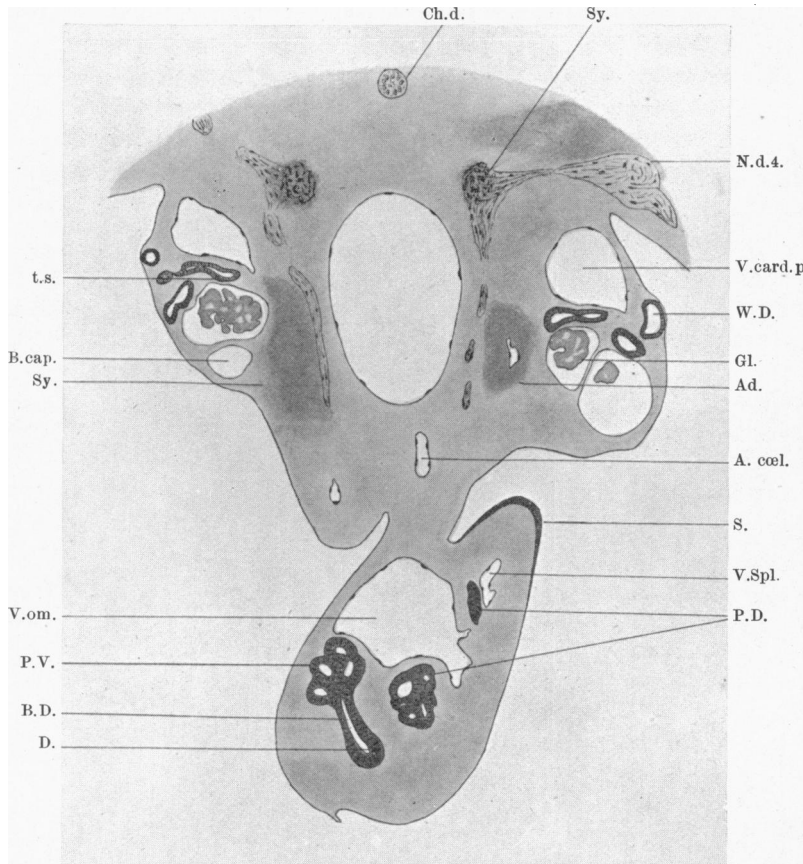


FIG. 18.  $\times 65$ .

ing terminal portion of the omphalo-mesenteric vein (fig. 15). The vena hepatica revehens communis is continued caudally into liver sinusoids lying in the dorsal margin of the liver, and through these is in connexion with a definite venous vessel which runs caudalwards in the border line between the liver tissue and the mesoderm bounding it dorsally, to the right of the recessus mesentericus and in the right leaf of the dorsal mesogastrium, *i.e.* in the caval mesentery. More posteriorly it leaves the dorsal surface of

the liver, passes dorsal to the hiatus communis recessuum and comes to lie ventro-mesial to the right mesonephros, and comes into relation with the anterior extension of the subcardinalis system, with which it is connected by anastomosis. We have therefore here present a definite anlage of the inferior vena cava (compare figs. 15-18). A single pulmonary vein opens into the caudal part of the atrium to the left of the lower end of septum I. It gets a large branch from the mesoderm in front of the left lung anlage and smaller tributaries from the right.

*Note on the Blood.*—On Plate II. fig. 7, *a*, *b*, and *c*, are pictured the main characters of three nucleated red blood cells from the spatium septo-valvulare of the heart. The nucleus shows a gradation in the density of its network—"ichthyoid" and "sauroid" types of Minot. The size of the nucleus in relation to the size of the cell-body diminishes from *a* to *c*, while the three cells show a varying depth of colour in their protoplasm. In general it may be stated that practically all the types of red cell are present which have been described by Maximow for mammalian embryos. His "primitive blood-cells" or the "primitive mesamœboids" of Minot could not be definitely identified. In *a* we have a typical "normoblast" of Maximow, and *c*, according to his interpretation, is a "primitive erythroblast," while *b*, in as far as the deep red coloration of its protoplasm is concerned, must be classed as a "megalo-blast." Mitotic figures occur frequently in the nucleated red cells of the blood-stream. Non-nucleated plastids occur but sparingly in the embryonic vessels, but beneath the amnion in the distal part of the cord and in the "chorionic cavity," artificially produced by a stripping off of the amnion from the surface of the cord, numerous non-nucleated red cells are found in company with nucleated normo- and megaloblasts. These are much smaller than the embryonic blood cells proper and very irregular in shape, and have resulted probably from an extravasation of maternal blood from the placenta. Plate II. fig. 7, *d*, represents three leucocytes ("lymphocytes" of Minot) with typical reniform nuclei which contain numerous relatively large chromatin aggregations. The nuclei are basophile and stain blue in the sections. The protoplasm is clear, with a vacuolated appearance, and is non-granular. Such cells are relatively few in number and always occur in groups, in which however the cell boundaries are distinct. Schridde, in his paper on the development of the blood in early human embryos, asserts that up to a stage of 12 mm. no leucocytes are present in the blood-stream, being first formed in the liver when that organ enters on its blood-forming function. Maximow strongly opposes this view, and in the face of the present findings the position of Schridde would appear quite untenable.

## THE UROGENITAL SYSTEM.

*The Mesonephros* is situated between the 8th cervical and 3rd lumbar segments inclusive. On the left side thirty-seven tubules are present, all of which are S-shaped and provided with Bowman capsules and have collecting tubules opening into the primary excretory duct. On the right side occur thirty-eight complete tubules with capsules and collecting tubules opening into the duct, and posterior to these is a 39th and rudimentary member of the series. The latter is in the form of a small, more or less olive-shaped epithelial body, containing a lumen and with a solid pole abutting very obliquely against the mesial aspect of the Wolffian duct without opening into it. According to Félix, no new tubule anlagen are added at the caudal end after the 7-mm. stage; and since this tubule scarcely corresponds in its relations or appearance either with a normally developing or with a normally degenerating tubule, the structure in question is probably to be regarded rather as of an abortive nature. The more caudal tubules on both sides cannot be said to have completed their development, inasmuch as the capsules here consist of widely open saucer-like structures, in contrast to the double-sphere form with only a small aperture for the glomerular vessels seen in the more anterior members of the series. On the left side there are no definite signs of degeneration either cranially or caudally, except in the somewhat shrunken appearance of the more anterior glomeruli and their smaller size in relation to the comparatively large capsule. For the right side the same statement holds good with regard to the anterior tubules, but here there is further to be observed an involution of the two anterior Wolffian arteries. The first possesses no apparent lumen, consisting merely of a cord of cells connecting the capsule with the aorta, while in the case of the second no opening into the aorta could be made out. This negative finding may be due to a slight folding in this region, but the artery is nevertheless far from normal and its glomerular plexus less evident than those of its caudal neighbours. The primary excretory duct is anteriorly and on either side continuous at an angle with the first collecting tubule, and runs caudally close beneath the coelomic epithelium lateral to the Wolffian tubules (figs. 15-21). At its caudal end it curves towards the middle line and runs internal to the origin of the umbilical arteries to end by opening into the dorso-lateral aspect of the urogenital cloaca (fig. A). At the junction of each collecting tubule the duct undergoes a localised enlargement (compare the two sides of fig. 18). Towards the caudal end of the mesonephros the enlargements run together, and the duct appears in consequence as a tube of much larger calibre. Caudal to the last mesonephric tubule it suddenly narrows,

and remains relatively small down to the point of origin of the ureteric outgrowth. Posterior to this point it expands into a funnel which is

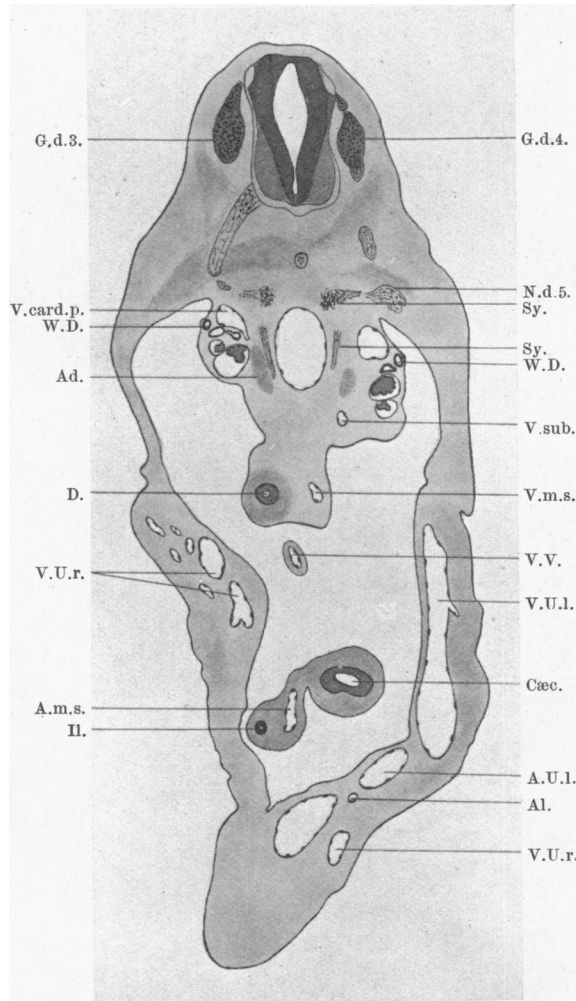


FIG. 19.  $\times 25$ .

still definitely marked off from the cloacal lumen. No pronephric rudiments are to be seen on either side. The vessels of the mesonephros have been fully described in the sections on the circulatory system.

*The Metanephros.*—The ureter arises from a somewhat lateral as well

as dorsal aspect of the primary excretory duct of the mesonephros a short distance from the opening of the latter into the cloaca (fig. A). The

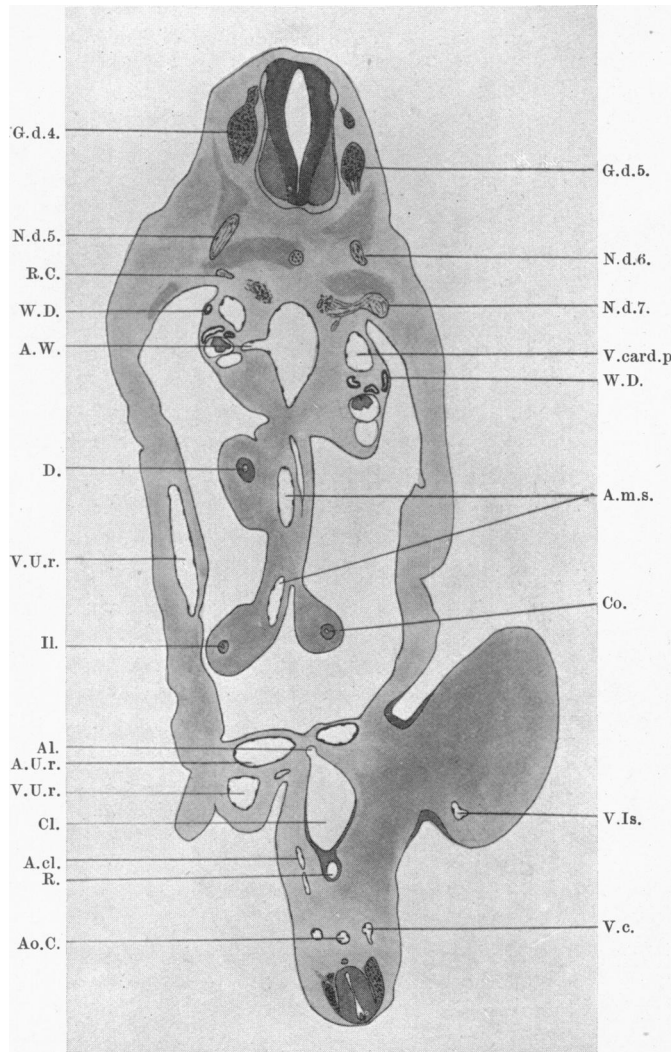


FIG. 20.  $\times 25$ .

renal pelvis is differentiated from the ureter proper and has the form of a flask-shaped terminal swelling slightly flattened laterally, the whole anlage being curved with its apex directed orally as well as dorsally (see fig. A).

The pelvis is capped by a layer of very dense mesodermal tissue in which the nuclei are arranged in a markedly radiating manner. From this cap a thick cord of condensed mesoderm stretches forward to a point caudo-

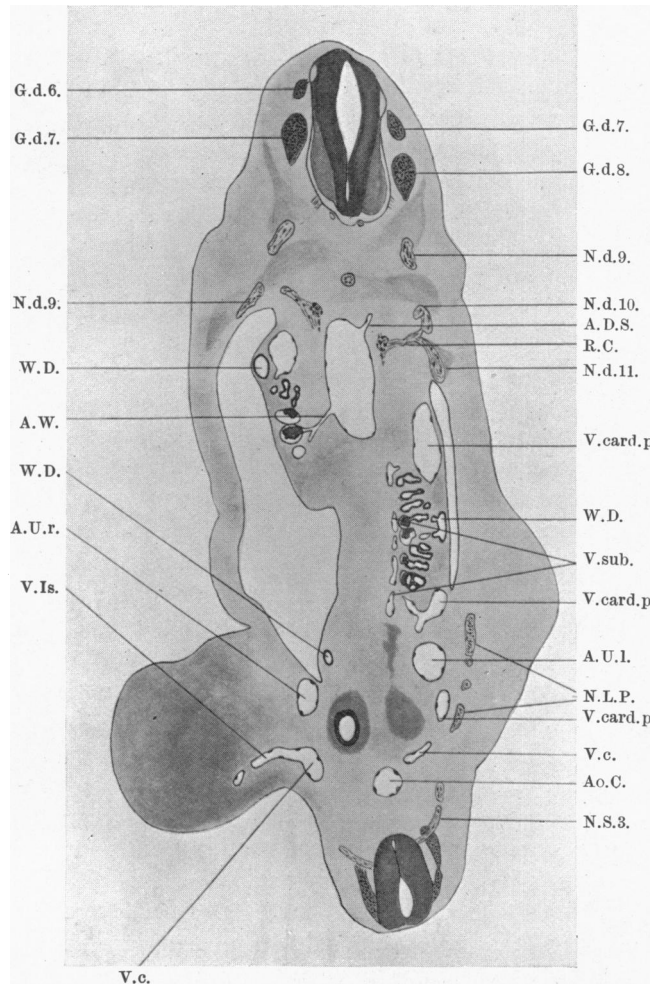


FIG. 21.  $\times 25$ .

mesial to the tail of the mesonephros and ends close to the latter, being separated from it only by the large anastomotic vessel which here connects the subcardinal with the posterior cardinal vein (fig. 21). The subcardinal is continued caudally dorsal to this condensation, as has already been mentioned in connexion with that vein.

## THE GENITAL EPITHELIUM AND "GENITAL CELLS."

A germinal epithelium exists only in a very early and indefinite condition. There is some thickening of the coelomic epithelium between the Wolffian ridge and the root of the mesentery in the lower dorsal region on either side, with some proliferation of its elements in a dorsal direction against the mesoderm. This thickening has no definite anterior or posterior boundaries, and passes gradually laterally and mesially into the unthickened area without any distinct line of demarcation. In connexion with the reproductive epithelium, however, mention may be made of a very characteristic type of cell found in the dorsal part of the mesentery and between this point and the germinal region at the lower dorsal levels. In Plate II. fig. 8, *a*, one of these cells is figured lying in the mesentery about midway between its base and the intestinal tube. Its large size and definite outline at once differentiate it from the surrounding mesoderm cells. The nucleus is regularly rounded and eccentric and contains a large irregular chromosome resulting from a clumping of the nuclear chromatin network (von Berenberg-Gossler), and divided into two portions, which, however, remain connected by a fine bridge. The cell-body contains a clear protoplasm with a generally vacuolated appearance, but in close contact with the nucleus and in the long axis of the cell is a close network—a more or less typical "Golgi-net"—containing a single dark spot, probably of the nature of a centrosome. In fig. 8, *b*, Plate II., a somewhat similar cell is shown, in which, however, the Golgi-net is absent and the chromosome in three portions. This cell was found between the Wolffian body and the root of the mesentery some distance dorsal to the coelomic epithelium. Fig. 8, *c*, is of a cell of the same type, but from amongst the cells of the proliferating genital epithelium. The cells here pictured, which occur only sparingly in the situations mentioned, closely resemble those which have for many years been described in the literature as "genital cells" for the various vertebrate classes, and their appearance at once suggests the possibility of their being of this nature. The origin of primitive "sex cells" from other sources than the coelomic germinal epithelium has long been an established fact, although observations in this direction on the human embryo have been very limited, and the question whether such cells are genetically continuous with the definitive genital cells has remained unsolved. Félix, recording the occurrence of "primary extra-regional genital cells" in human embryos of 2.5, 2.6, and 4.9 mm.—in the earlier stage in the neighbourhood of the cloaca, in the later stage in or under the coelomic epithelium near the root of the mesentery—states that in amniotes all the primary cells either disappear entirely or enter on



a latent stage with a possible later appearance as definitive secondary cells. Fuss (1912), on the other hand, in his work on the genital cells of man and mammals, traces the path of these cells from the entoderm of the yolk-sac to the genital region in later stages, and holds that inclusive of the human embryo the so-called "germinal epithelium" plays only a very unimportant rôle in the genesis of the sex-cells, and begins to proliferate only when the majority of the genital cells, coming originally from the yolk-sac entoderm, have arrived at their destination in the genital region. Von Berenberg-Gossler (1912) has further worked out and pictured the histogenesis of the primitive genital cells in the chick and embryo duck, and it is an interesting fact that the cell figured in our Plate II. fig. 8, *a*, is almost identical with those in his figures of three- to four-day embryos after staining with iron-haematoxylin. This author finds that cytological analysis provides no definite proof that these cells are in reality the ancestors of the male or female reproductive cells, and, with Fick, regards the peculiar clumping together of the nuclear chromatin as a "resting-network," associated with diminished functional activity. The suggestion that the appearance of such cells as those here described for the present embryo is due merely to an enlargement and modification of ordinary mesoderm cells in preparation for mitosis is at once disposed of by the striking analogy which exists between these cells, and those of the chick, in which mitotic division is absent or exceedingly rare. Furthermore, where mitotic division occurs in the surrounding mesoderm, as it frequently does, the cell in this case, although assuming a rounded-off appearance and increase in bulk, as described by Maximow, never simulates the cells in question either in size or histological character. That, finally, they are not to be identified as of the nature of "Wanderzellen" of Maximow is shown by the regular rounded nucleus which they in every case possess.

#### THE CONNECTIVE TISSUES.

The chorda dorsalis extends from a short distance behind the hypophysis (fig. 5) to the tip of the tail. It is in contact with the epithelium of the roof of the pharynx. On cross-section it shows a thick homogeneous membrane enclosing a clear, apparently homogeneous protoplasm in which the nuclei are arranged in a single circle in the middle thickness. No cartilage or "pre-cartilage" is present in the membranous skeleton. Parts of the base of the skull are indicated in membrane, viz. the pars petrosa, as well as the vertebral bodies with costal processes and a few ribs. The anlage of Meckel's cartilage has been mentioned above in connexion with the mandibular nerve. Three head segments and thirty-six or thirty-seven body segments are present. In all three of the former distinct differentiated

muscle fibres are to be observed, as is the case with the body segments as far caudal as the fourth sacral.

#### THE BODY-CAVITIES.

The lateral halves of the pericardium communicate with each other in front anterior and ventral to the truncus arteriosus. Soon, however (fig. 7), the two become separated by the mesoderm surrounding the truncus and bulbus, which extends from the dorsal to the ventral wall of the pericardium. Its dorsal attachment, or anterior section of the dorsal mesocardium, is little more than the mesoderm surrounding the truncus and sixth aortic arch as these leave the pericardial cavity. Ventrally the bulbus is closely applied to the anterior pericardial wall through about thirty sections ( $10\mu$ ), and partial fusion occurs (fig. 7). There is in every section, however, a broken line of epicardium demarcating the two, so that the fusion is very incomplete, and one cannot speak of a true ventral mesocardium in this region. Behind the point where the anterior section of the dorsal mesocardium ceases the broad tracheal ridge juts dorsally into the pericardium, and gradually increasing in dorso-ventral height it finally fuses, from the tracheal bifurcation caudally, with the dorsal surface of the heart to form the main or caudal section of the dorsal mesocardium (figs. 9 and 10). From this point the dorsal wall of the pericardium, with which the dorsal mesocardium is continuous on either side, slopes rapidly ventrally and caudally, and is here formed by the comparatively smooth antero-ventral surface of the septum transversum. On either side of the tracheal ridge ("bourrelet mésentérique" of Brachet) anteriorly is a broad groove without any definite lateral boundary (on left side of fig. 8). Traced backwards this groove gradually deepens and narrows ("gouttière pleuro-péricardique" of Brachet) and a well-marked ridge appears to demarcate it laterally (right side of fig. 8). More caudally still the groove becomes bounded on its lateral aspect and later ventrally also by the duct of Cuvier as it sweeps caudally and mesially, and by the mesodermal membrane which connects that vessel with the body-wall (fig. 9). The groove ("gouttière pleurale") is, however, still incomplete below, inasmuch as its appearance in the above figure as a closed "cavity" is due to the presence of a portion of the atrial wall, and it is only when the mesoderm on the dorsal and mesial aspect of the duct of Cuvier fuses with the dorsal mesocardium and thus completes the pleuro-pericardial membrane that the pleural cavity is fully shut off from the pericardium proper (fig. 10). Between the anterior and posterior sections of the dorsal mesocardium the pleuro-pericardial grooves communicate with each other, at first freely but more caudally through a slit-like space between heart and tracheal swelling. The part played by the duct of Cuvier in bounding the

pleuro-pericardial opening can be well seen in figs. 8 to 11. The duct with its mesodermal connexion with the body-wall bounds the groove at first laterally and then later below, but the ridge thus produced, as Brachet and others have pointed out, does not constitute the anlage of the pleuro-pericardial membrane proper. From the mesial aspect of the duct of Cuvier at its oral and dorsal end a prominent ridge, already mentioned, consisting of condensed mesoderm with thickened epithelium and an irregular surface, extends oralwards and gradually moves on to the dorsal aspect of the pericardium, reaching in front the lateral part of the "bourrelet mésentérique." This is the anterior extension of the pulmonary ridge (Mall). Behind, it spreads out, first on the mesial, later on the dorsal aspect of the Cuvierian duct, and adds itself to the mesodermal membrane, connecting the latter with the body-wall, while, as Brachet has shown, it joins the mesoderm around the duct, by its active growth, with the dorsal mesocardium, and through this with the mesodermal lung anlage (fig. 10). It thus converts the pleuro-pericardial groove into a "cavity," and is connected at both ends with the mesoderm surrounding the lung, and can later, by active growth, complete the closure of the pleuro-pericardial opening. The pulmonary ridge being thus the true anlage of the pleuro-pericardial membrane, the duct of Cuvier lies at first in its lateral edge and later comes to hang from its ventral surface (fig. 10). Still later it leaves the pleuro-pericardial membrane altogether (fig. 11) to run along the lateral aspect of the dorsal mesocardium before entering this structure on its way to the sinus venosus. In other words, the "lateral mesocardium" and the pleuro-pericardial membrane are two distinct structures, the former bringing about a constriction of the pleuro-pericardial communication without taking any active part in the actual closing process. In figs. 10 and 11 the antero-lateral recess of the peritoneal coelom has appeared (on the right side of both figures), and here the pleuro-pericardial membrane forms a T-shaped junction with the pleuro-peritoneal membrane extending dorsally and the "pericardio-peritoneal membrane" ventrally and laterally. The latter is at no point a true membrane like the other two, being very much thicker, and constitutes in reality the anterior or dorsal edge of the septum transversum, in which, a few sections posteriorly (fig. 12), liver trabeculae appear. It is thus seen that the pleuro-pericardial membrane is itself a portion of the anterior edge of the septum. In fig. 11 the dorsal attachment of the pleuro-peritoneal membrane is the dorsal body-wall under the cardinal sinus; ventrally and mesially it is continuous with the dorsal surface of the septum transversum, through the pleuro-pericardial and "pericardio-peritoneal" membranes. It has spread out on its mesial surface the epithelium of the pulmonary ridge, and is partly made up of that structure.

Followed forward it is seen to be attached to the posterior aspect of the dorsal part of the duct of Cuvier (Brachet), as well as being continued orally from that level and mesially as the pulmonary ridge. Posteriorly it ends in a caudally directed free edge with dorsal and ventral prolongations which differ somewhat on the two sides. On the left side the dorsal prolongation, or dorsal pillar of Uskow, is the better marked, is continued into a ridge mesial to the anterior extremity of the Wolffian mesentery (fig. 12), and gradually fades away in this position. The ventral pillar is thicker and flattens out rapidly into the septum transversum, or, more correctly, is invaded and spread out by liver tissue so that it soon loses its ridge-like form. On the right side, where the right lobe of the liver has not reached the ventral pillar, the latter is high and sharp (fig. 13) and is continued back along the upper surface of the septum transversum. In general the pleuro-peritoneal membrane is situated in a sagittal plane, but is bulged laterally by the mesodermal lung anlage.

When the condition described above is compared, for instance, with that found in a 7-mm. embryo, in which, as Mall says, the pulmonary ridge "connects the dorsal end of the septum transversum with the Wolffian body," as is seen in the large Piper-Ziegler model of a 6.8-mm. embryo (1902); and when it is further considered that this ridge is the anlage of both pleuro-pericardial and pleuro-peritoneal membranes, it is possible to appreciate the full significance of Brachet's description (1897) in which he regards both anlagen as "spreading so to speak from one point to develop in different directions, one caudal and the other cranial."

The liver bulges from the dorsal surface of the septum transversum, reaching farther forward on the left side, where it ends in a wing-like expansion extending into the antero-lateral recess (fig. 11). On the right side, though not extending so far forward, it fills up most of the anterior portion of the greater peritoneal sac. Where the large vena umbilicalis sinistra enters the liver from the body-wall the ventral mesentery may be said to commence, and it is continued caudally from the posterior aspect of the vein as a thin membrane (fig. 17) connecting mesentery and body-wall for about twenty sections ( $10\mu$ ). Behind this it is produced as dorsal and ventral pillars on the mesenteric edge and ventral body-wall respectively as far back as the umbilical coelomic diverticulum.

Fig. 17 shows the incomplete foramen of Winslow, or hiatus communis recessuum, through which the lesser peritoneal cavity has a wide communication with the greater. The hiatus is bounded above by the point of separation of the caval mesentery from the dorsal surface of the liver, behind by the caval mesentery with the early inferior vena cava, in front by the posterior surface of the right lobe of the liver, and is widely open

to the right and below. From this opening the lesser peritoneal cavity extends orally and expands in three main directions: (a) ventrally between the stomach and right lobe of the liver, recessus hepato-entericus; (b) to the left over the dorsal aspect of the pylorus and distal part of fundus, r. mesenterico-entericus; and (c) orally, partially separating the lower end of the oesophagus and the stomach from the right lung anlage, r. pneumato-entericus (*cf.* figs. 13, 15, 16, and 17).

Caudal to the origin of the pancreas the dorsal mesentery follows the main intestinal torsion, and merits no special description (figs. 19 and 20).

My thanks are due to Geheimrat Professor Wiedersheim for permitting me to work in his laboratory over an extended period, and for placing the resources of the Institute at my disposal; to Professor Keibel for the loan of his embryo and continuous supervision and helpful criticism during the course of the work; and to Dr von Berenberg-Gossler for many valuable suggestions.

FREIBURG IN BREISGAU,  
*April* 1914.

#### LIST OF PRINCIPAL ABBREVIATIONS.

A.br. = brachial artery.	p. = profunda.	s. = superficialis.	Ao. = aorta.	A. = aortic arch.	C. = caudal.	d. = dorsal.
A.c. arteria centralis (of spinal cord).			Ap. appendix.			
A.c.e. carotis externa.			At.c. atrial canal.			
A.c.i. carotis interna.			B.A. bulbus arteriosus.			
A. cœl. cœliac artery.			B.cap. Bowman's capsule.			
A.cl. cloacal branch of caudal aorta.			B.D. common bile duct.			
A.D.S. dorsal segmental artery.			B.E. eparterial bronchus bud.			
A.f.b. artery of fore-brain (a. cerebri ant. et med.).			B.L. lateral bronchus bud.			
A.m.s. arteria mesenterica superior.			B.S. bulbar swelling. A and B = proximal, 1 and 3 = distal.			
A.P. pulmonary artery. l. = left.			B.St. stem bronchus.			
		r. = right.	Cæc. cæcum.			
A.r.d. a. radicularis dorsalis.			C.D. cystic duct.			
A.r.v. a. radicularis ventralis.			Ch.d. chorda dorsalis.			
A.S. subclavian artery.			Cl. cloaca.			
A.Spl. splenic artery.			Co. colon.			
A.U. umbilical artery.			D. duodenum.			
A.V. vertebral artery.			D.A. ductus arteriosus.			
A.W. Wolfian artery.			D.br. ductus branchialis.			
Ad. adrenal cortex.			D.E. ductus endolymphaticus.			
Al. allantois.			Ep.B.III. epithelial body of third pharyngeal pouch.			

- F.B. = fore-brain.  
 G.B. gall-bladder.  
 G.F. Froriep ganglion.  
 Gl. Wolffian glomerulus.  
 G.S. spinal ganglion.  
 G.c. cervical ganglion. d. = dorsal.  
     l. = lumbar. V. = Trigem-  
     inal.  
 H.B.r. roof of hind-brain.  
 H.C.R. hiatus communis recessuum.  
 H.D. hepatic duct.  
 Hem. cerebral hemisphere.  
 Hy. hypophysis.  
 Il. ileum.  
 J. organ of Jacobson.  
 K. kidney.  
 L. liver.  
 La. larynx.  
 M.B. mid-brain.  
 M.p.p. pleuro-pericardial membrane.  
 M.p.pt. pleuro-peritoneal membrane.  
 Mx. maxilla.  
 My.O.3. third occipital myotome.  
 N.acc. accessory nerve.  
 N.B.P. brachial plexus.  
 N.c. cervical nerve.  
 N.Ch.T. chorda tympani.  
 N.d. dorsal nerve.  
 N.E. nervus epibranchialis.  
 N.La. laryngeal branch of N. X.  
 N.L.P. lumbar plexus.  
 N.Md. mandibular nerve.  
 Mx. maxillary n.  
 N.O. ophthalmic n.  
 N.ph. phrenic n.  
 N.ps. superficial petrosal n.  
 N.rad. radial n.  
 N.S. sacral n.  
 N.X. vagus n.  
 N.XII.d. descendens hypoglossi.  
 Neu. neuromere.  
 N.L. naso-lacrimal groove.  
 O. oesophagus.  
 OP. optic anlage.  
 OT. otic vesicle.  
 P. pericardium.  
 P.D. = dorsal pancreas.  
 Ph.p. pharyngeal pouch.  
 Pl. placode.  
 P.R. pulmonary ridge.  
 P.U. pillar of Uskow. d. = dorsal.  
     v. = ventral.  
 P.V. ventral pancreas.  
 Py. pylorus.  
 R. rectum.  
 R.C. ramus communicans.  
 R.H.E. recessus hepato-entericus.  
 R.M.E. „ mesenterico-entericus.  
 R.P.E. „ pneumato-entericus.  
 S. spleen.  
 S.A.P. septum aortico-pulmonale.  
 S.B.D. distal bulbar septum.  
 Sp.s.v. spatium septo-valvulare.  
 S.s. sinus sagittalis.  
 S.v. sinus venosus.  
 Sy. sympathetic cord and ventral  
     branches.  
 T. trachea.  
 T.A. truncus arteriosus.  
 Th. thyroid anlage.  
 t.s. secreting Wolffian tubule.  
 Ty. thymus anlage.  
 V.c. caudal vein.  
 V.Cu. Cuvierian vein.  
 V.C.I. vena cava inferior.  
 V.Hep. hepatic vein. c. = common.  
     l. = left. r. = right.  
 V.Is. ischiadic vein.  
 V.m.s. superior mesenteric vein.  
 V.om. omphalo-mesenteric v.  
 V.p. pulmonary v.  
 V.r.a. ramus arcuatus.  
 V.r.ang. ramus angularis.  
 V.S. subclavian vein.  
 V.sub. subcardinal v.  
 V.T.E. thoraco-epigastric v.  
 V.U. umbilical vein.  
 V.Ul. ulnar vein.  
 V.V. venous valve.  
 W.D. Wolffian duct.  
 W.R. Wolffian ridge.

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#### EXPLANATION OF PLATES I. AND II.

Fig. 1. Photograph of the Embryo.  $\times 4$  ca.

Fig. 2. Drawing of a portion of a section containing a "cellular ramus communicans." Ao., aorta; N.c.3, third cervical nerve.  $\times 1120$  ca.

Fig. 3. Drawing of a model of the right olfactory region, seen from below and somewhat from the right side. Mid.l., middle line; Mx., maxilla; N.L., nasolacrimal groove; OP., optic anlage.  $\times 40$  ca.



Fig. 4. Drawing of a portion of a section passing almost horizontally through the upper part of the third pharyngeal pouch. Ep.B.III., anterior wall or anlage of the epithelial body of the pouch; Ty., posterior wall or thymic anlage.  $\times 1120$  *ca.*

Fig. 5. Drawing of a model of the pancreatic outgrowths with the biliary ducts and a portion of the right lobe of the liver. D., duodenum; G.B., gall-bladder; H.D., hepatic duct; L., liver; P.D., dorsal pancreas; P.V., ventral pancreas; St., stomach; V.om., omphalo-mesenteric vein; V.v., vitelline vein; V.m.s., superior mesenteric vein.  $\times 75$ .

Fig. 6. Drawing of a model of a part of the intestinal loop, with a portion of the superior mesenteric artery. A.m.s., superior mesenteric artery; Ap., appendix; Co., colon; Il., ileum.  $\times 75$ .

Fig. 7. Drawing of some blood-cells from the spatium septo-valvulare of the heart. *a*, *b*, *c*, erythrocytes; *d*, leucocytes.  $\times 1500$  *ca.*

Fig. 8. Drawing of three "genital cells." *a*, cell lying in the mesentery, from the lower dorsal region; Cœ., cœlomic epithelium; *b*, cell from the mesoderm dorso-mesial to the cœlomic epithelium, with a neighbouring mesoderm cell; *c*, cell from the left genital region.  $\times 1120$  *ca.*

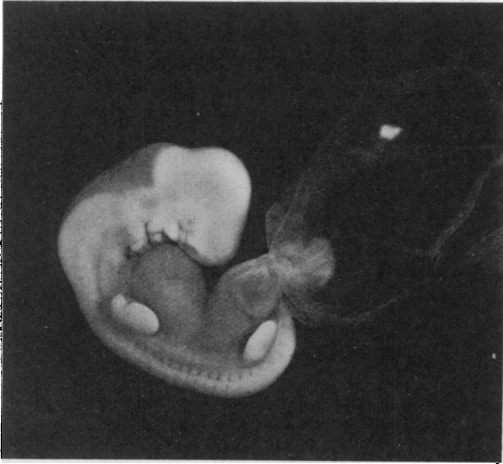


FIG. 1.—Human embryo of 8.5 mm.  $4 \times ca.$

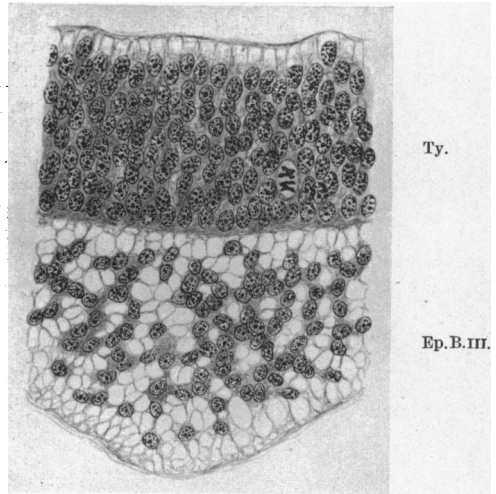


FIG. 4.  $\times 1120 ca.$

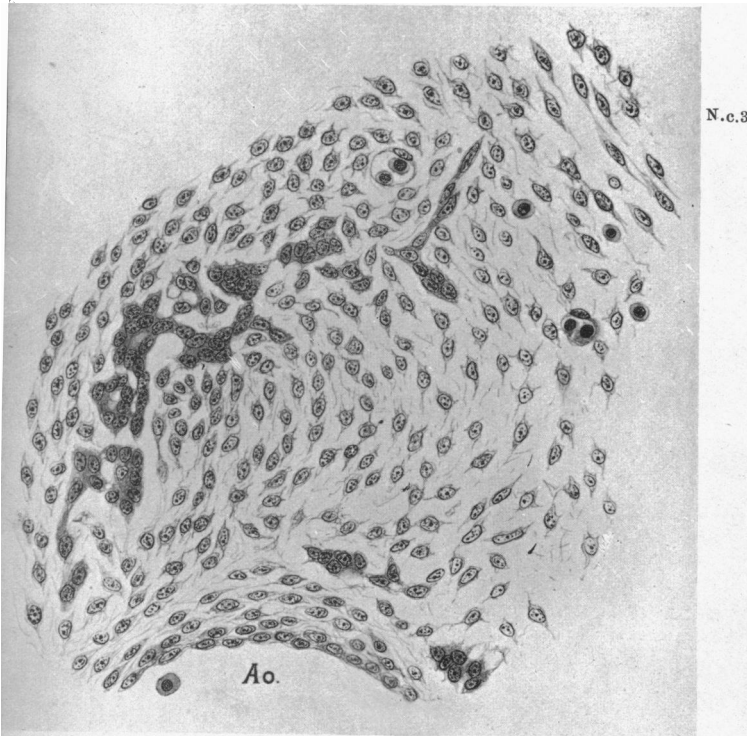


FIG. 2,  $\times 1120 ca.$

*Pinxit Schilling.*

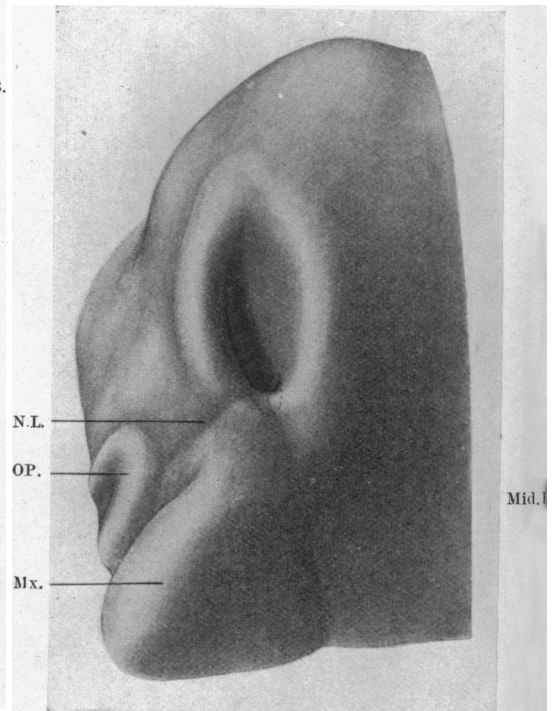


FIG. 3.  $\times 40 ca.$

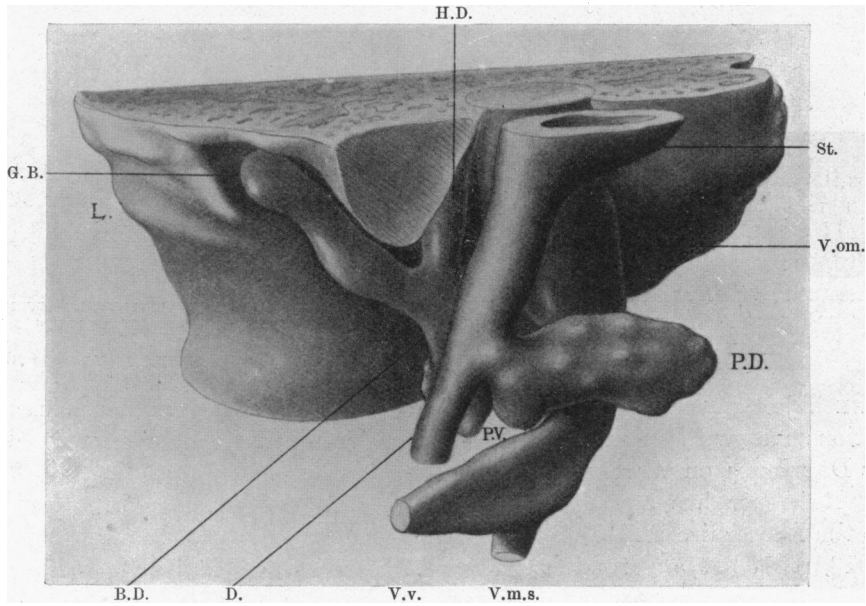


FIG. 5.  $\times 75$ .

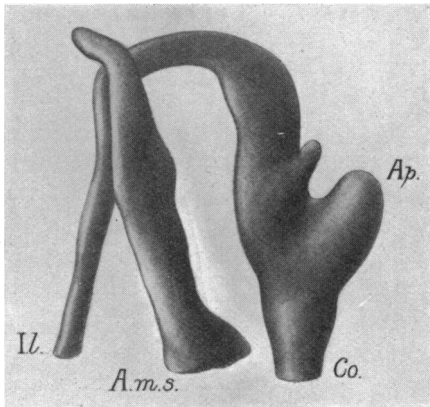


FIG. 6.  $\times 75$ .

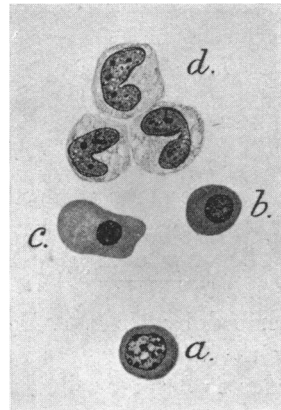


FIG. 7.  $\times 1500$  ca.

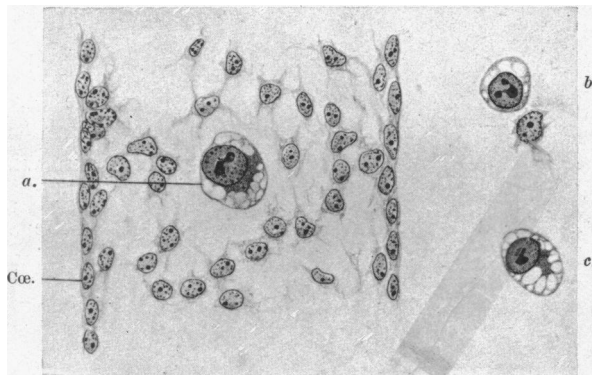


FIG. 8.  $\times 1120$  ca.